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RISK ASSESSMENT METHODOLOGY FOR HAZARDOUS WASTE MANAGEMENT

By

Edward W. Lawless

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PREFACE

Results are presented in this report of a study by Midwest Research Institute (MRI) entitled "Risk Assessment Methodologies for RCRA," on Task Order No. 85-ED1-ANF, under Contract No. EQ4C15 "Basic Ordering Agreement for Environmental Studies, Research, and Analysis," MRI Project No. 8170-L(4). The work was performed for the Office of Policy Analysis, Office of Policy, Planning and Evaluation, U.S. Environmental Protection Agency. Dr. Ann N. Fisher was EPA Task Officer, and Dr. William Mills was Technical Representative for the Council on Environmental Quality on this task.

The results herein draw substantially on related research at MRI for the Office of Policy Analysis, under EPA Contract Nos. 68-01-6621 (MRI Project Nos. 7549-L(2) and 7549-L(12)) and on 68-01-6558 (MRI Project No. 8151-L). A report of that work, "Comparison of Risks and Costs of Hazardous Waste Alternatives: Methods Development and Pilot Studies," is available through the National Technical Information Service (NTIS No. PB86-158,912). Dr. Fisher was Project Officer or co-Project Officer with Ms. Jeanne Briskin throughout the earlier work.

Many people contributed to this study. Mr. Thomas L. Ferguson, then Head, MRI's Process Assessment Section, was Project Leader for all the research under the earlier related contracts noted above. Dr. Thomas W. Lapp, Senior Chemist, was a major contributor to that research. Other MRI contributors to the methodology development included: Mr. Christopher J. Cole, Assistant Environmental Scientist and Mr. Gary L. Kelso, Senior Chemical Engineer in the areas of source assessment and control technology assessment; Mr. Phillip J. Englehart, Associate Environmental Scientist, Mr. Michael K. Snyder, Associate Environmental Scientist, and Mr. Fred C. Hopkins, Associate Environmental Scientist in environmental transport modeling; Dr. Harry V. Ellis, MRI consultant in toxicology and environmental health and Dr. Dennis Y. Takade, MRI consultant in toxicology and environmental health in health effects modeling; and Dr. Jairus D. Flora, Jr., Principal Statistician in uncertainty analysis. Dr. John Doull, Professor of Pharmacology and Toxicology, University of Kansas School of Medicine, and Dr. Kenny S. Crump, K.S. Crump and Company, Inc., assisted on health risk estimation methods, and Mr. William L. Murphy Rohrer of Pope-Reid Associates on landfill failure and groundwater modeling. Professor Harold Orel, Department of English, University of Kansas and MRI consultant in technical writing, reviewed the draft manuscript of this report and made many helpful suggestions.

Individuals from several offices of EPA and from other organizations provided helpful references, materials, and review comments on reports prepared during the earlier studies. We are pleased to list names and affiliations of known reviewers in the Acknowledgments. Particular appreciation is expressed to the members and consultants of the EPA Science Advisory Board's Environmental Engineering Committee, Waste Banning Subcommittee. They reviewed and discussed with the study team a proposed general method for comparing the risks of alternative hazardous waste disposal technologies and pilot tests of the method. Questions and suggestions by all of the reviewers have contributed substantially to the quality of these results.

Although this study was made in support of EPA's needs to assess the risks associated with alternative hazardous waste management approaches, MRI hopes that the research and methodology described will be useful also in other environmental regulatory processes and in other decision making applications.

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September 23, 1988

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ABSTRACT

A methodology is described for systematically assessing and comparing the risks to human health and the environment of hazardous waste management alternatives. The methodology selects and links appropriate models and techniques for performing the several portions of the comparative assessment process. The selection of component methods was based on intensive review and evaluation of the technical and science policy literature, particularly works on environmental transport modeling, health effects modeling, and risk assessment and risk management concepts. The goal of the methodology is to develop both best estimates of the risks to potentially exposed individuals and populations for each identified waste management alternative, and also estimates of the upper and lower limits of the risk range at one or more confidence levels, considering both random and systematic sources of uncertainty. The methodology as presently developed is oriented toward site-specific assessments of alternative treatment, storage, and disposal facilities, and contains seven major steps: (1) Source Assessment (hazard characterization); (2) Environmental Transport and Fate Analysis; (3) Exposure Prediction; (4) Health and Environmental Effects Analysis; (5) Adverse Impact Estimation and Summation for Exposed Individuals and Populations; (6) Uncertainty Analysis; and (7) Report and Compare Results as Appropriate. Uncertainties for each step are aggregated to yield the uncertainty range about the best risk estimate. An extensive bibliography is included. Careful appraisal of the concepts of the methodology and demonstration of its utility in decision making are now needed, particularly in cases where alternative remedial actions are being considered for existing hazardous waste sites.

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SUMMARY

This report presents the results of a study performed by Midwest Research Institute (MRI) for the U.S. Environmental Protection Agency (EPA) in support of EPA's needs to assess and compare the risks and benefits to human health and the environment of alternative hazardous waste management technologies and standards. The research had four intermediate objectives:

a. To identify the necessary component steps and interrelationships of a risk assessment methodology for hazardous waste decision making

b. To identify, review, and evaluate available techniques and models that might be used for key portions of this methodology

c. To identify the most generally applicable, efficient, and scientifically defensible techniques and models for each step

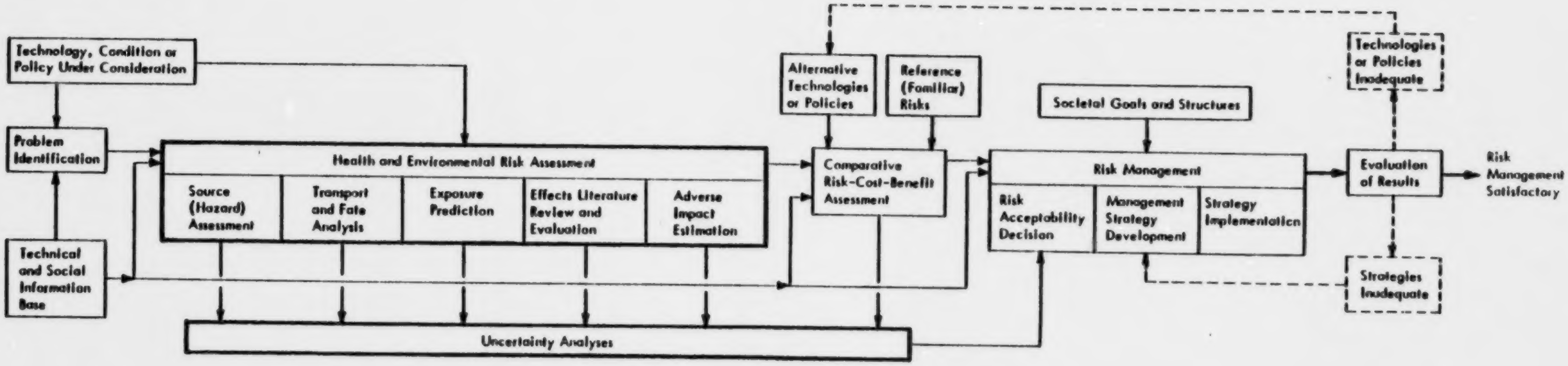
d. To link selected component methods into a flexible general methodology that should provide support for a range of regulatory decisions involving hazardous wastes

The overall goal was to develop a methodology that could enable EPA to compare both the best estimates of the risks of specified waste management alternatives and the explicit uncertainties associated with these best estimates.

Approach

A goal of our risk assessment methodology was to incorporate techniques and models that will yield scientifically defensible comparative assessments, and to avoid mixing in components more properly reserved to the risk management portions of the overall regulatory process. Careful consideration was given to how the components were defined and how they were related. The terminology adopted in this study was systematically selected following an extensive review and evaluation of the evolving and still widely varying nomenclature in use in the literature on risk assessment and risk management. A compatible, self-consistent set of definitions were developed that reflect the best of recent usage in the several disciplines associated with risk assessment/management concepts, both in the United States and internationally. A framework for the assessing and managing of technological risks in general was developed as shown in Figure S-1. (The health and environmental risk assessment and uncertainty analysis portions that are the subject of this report are within the heavy lines.)

Several important objectives and guidelines were identified for fitting a methodology for comparative risk assessment of hazardous waste management alternatives within this framework:


Technology, Condition or Policy Under Consideration
Problem Identification
Technical and Social Information Base
Health and Environmental Risk Assessment
Source (Hazard) Assessment
Transport and Fate Analysis
Exposure Prediction
Effects Literature Review and Evaluation
Adverse Impact Estimation
Uncertainty Analyses
Alternative Technologies or Policies
Reference (Familiar) Risks
Comparative Risk-Cost-Benefit Assessment
Societal Goals and Structures
Risk Management
Risk Acceptability Decision
Management Strategy Development
Strategy Implementation
Technologies or Policies Inadequate
Evaluation of Results
Strategies Inadequate
Risk Management Satisfactory

Source: MRI

Figure S-1 - Framework for Assessing and Managing Technological Risks

- The approach should be applicable to a range of potential regulatory decisions, but should not focus on making waste management decisions on a national level on specific wastes, specific waste sources, or specific kinds of waste treatment, storage and disposal facilities (TSDFs). The methodology should be testable, however, on specific wastes and TSDF technologies at specific sites.

- The methodology should be sufficiently flexible to address different hazardous wastes, TSDF technologies, modes of toxicant release and transport, exposure conditions, and health or environmental effects.

- The methodology should be applicable to a range of TSDF technologies, including: landfills; surface impoundments; surface spreading; storage in piles or containers; deep well injection; chemical and biological treatments; incineration on land or at sea; and combustion in boilers.

- The assessment of each option should consider all kinds of releases, multimedia environmental transport, and health and environmental effects (not just carcinogenicity, for example) for the life cycle of the technology or beyond if there are long term effects. Comparable contributing factors need to be treated comparably for each option.

- The methodology should yield quantitative results when necessary data are available and yield the most useful results possible when data (or the time and resources needed to compile data) are limited.

- The methodology should yield information on the most likely outcomes for each option, and also on the uncertainties in such estimates for all options considered.

Failure to be comprehensive and consistent throughout the assessment could lead to decisions that are less protective of health and the environment, and possibly also more costly to society than another decision would have been. Assessments involving mixed chemical wastes or disposal options that could lead to exposures to different chemicals with different health effects must be particularly careful to avoid inconsistent analysis that could lead to perverse decisions.

The Methodology

The methodology for assessing the health and environmental risks of hazardous waste management alternatives depends on four fundamental assumptions: (a) sequential analysis steps can be defined and linked to provide an overall assessment of the health and environmental risks of hazardous waste management alternatives; (b) each step can be performed by utilizing a combination of scenarios, available or estimated data, and predictive models;

(c) best "point" estimates of the risks can be obtained by using the most likely case assumptions, input data, and predictive models throughout, rather than intentionally "conservative" or "optimistic" choices; and (d) upper and lower confidence limits of the overall risk can be obtained by first estimating the uncertainties from both random and systematic sources of error in the assumptions, input data and models, and then aggregating or integrating the uncertainties across the risk assessment process.

Seven major methodological steps can be identified:

- Source Assessment (hazard characterization)
- Environmental Transport and Fate Analysis
- Exposure Prediction
- Health and Environmental Effects Literature Base Evaluation and Model Development
- Adverse Impact Estimation and Summation for Exposed Individuals and Populations
- Uncertainty Analysis
- Reporting and Communication of Results and Conclusions

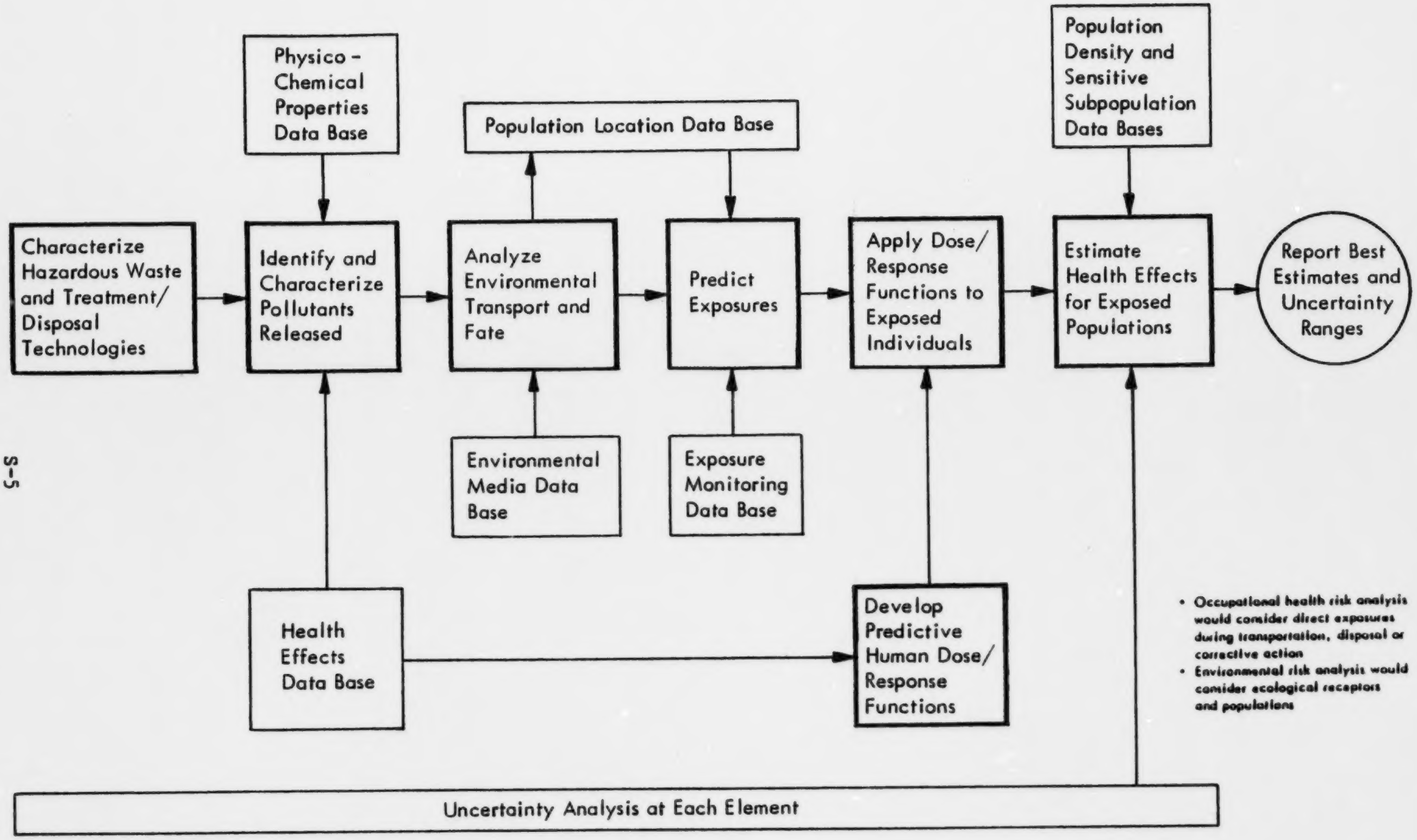
The interrelationships of these steps and supporting elements are shown systematically in Figure S-2. Activities involved in these steps are summarized below.

1. Source assessment (hazard characterization) requires characterization of the source of environmental contaminants, including:

- Identify chemicals present
- Identify preliminarily their physical, chemical, and biological properties of concern
- Analyze the technologies and practices that may result in release of contaminants to the environment and identify release points and routes
- Quantify source strength, i.e., the rate, concentration, quantity, and form of hazardous constituent released

A schema for assessing sources is given in Figure S-3.

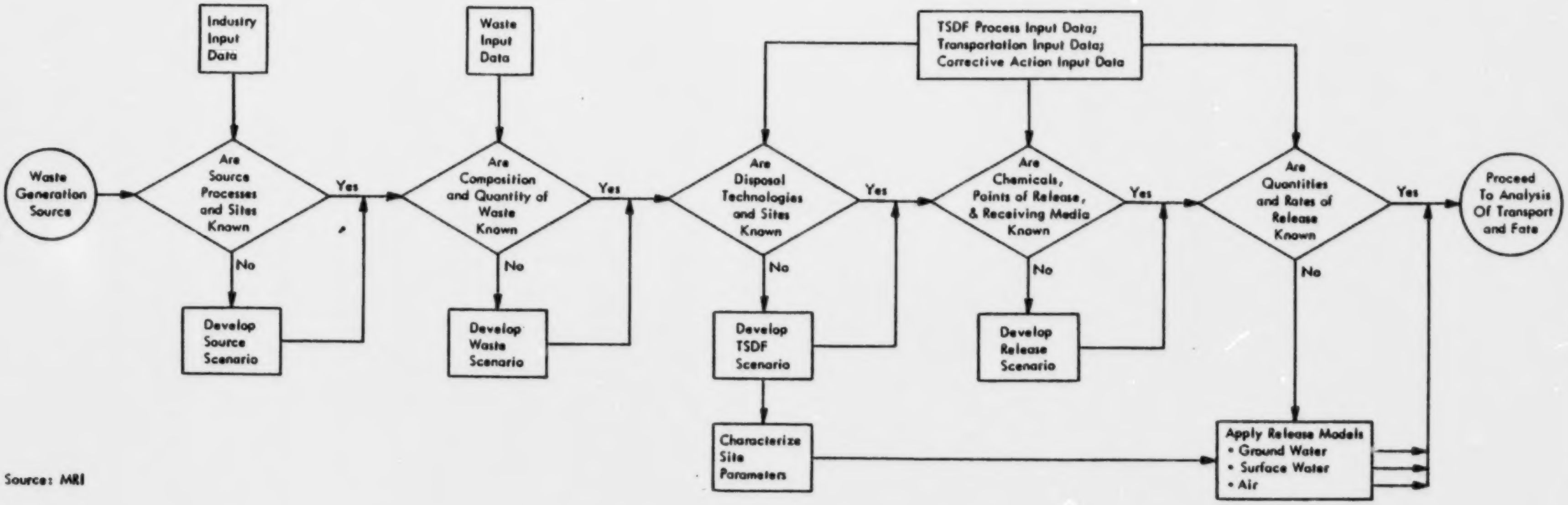
2. Environmental transport and fate analysis involves estimation of the manner in which the contaminants move and react in the environment, including:


Physico - Chemical Properties Data Base
Population Location Data Base
Population Density and Sensitive Subpopulation Data Bases
Characterize Hazardous Waste and Treatment/ Disposal Technologies
Identify and Characterize Pollutants Released
Analyze Environmental Transport and Fate
Predict Exposures
Apply Dose/ Response Functions to Exposed Individuals
Estimate Health Effects for Exposed Populations
Report Best Estimates and Uncertainty Ranges
Environmental Media Data Base
Exposure Monitoring Data Base
Health Effects Data Base
Develop Predictive Human Dose/ Response Functions
Uncertainty Analysis at Each Element

- Occupational health risk analysis would consider direct exposures during transportation, disposal or corrective action
- Environmental risk analysis would consider ecological receptors and populations

Source: MRI

Figure S-2 - Elements in Health Risk Assessment of Hazardous Waste Disposal Methods


Waste Generation Source
Industry Input Data
Are Source Processes and Sites Known
Yes
No
Develop Source Scenario
Waste Input Data
Are Composition and Quantity of Waste Known
Yes
No
Develop Waste Scenario
TSDF Process Input Data; Transportation Input Data; Corrective Action Input Data
Are Disposal Technologies and Sites Known
Yes
No
Develop TSDF Scenario
Characterize Site Parameters
Are Chemicals, Points of Release, & Receiving Media Known
Yes
No
Develop Release Scenario
Are Quantities and Rates of Release Known
Yes
No
Apply Release Models
• Ground Water
• Surface Water
• Air
Proceed To Analysis Of Transport and Fate

Source: MRI

Figure S-3 - Schema for Assessing Hazardous Wastes as Sources of Environmental Pollution

- Identify major environmental transport routes and transformation pathways for chemicals of concern

- Estimate concentrations of chemicals (or their hazardous transformation products) along these routes over time

- Identify locations along these routes where the chemicals may reach susceptible populations

A schema for the selection of suitable models for analysis of pollutant transport in different media is given in Figure S-4.

3. Exposure prediction involves estimation of the degree to which pollutants reach humans or other organisms, including:

- Estimate numbers of people or organisms that may be contacted

- Predict frequency, intensity, and duration of the exposures that may occur for populations or subpopulations

4. Health and environmental effects analysis involves:

- Review intensively the literature on the health and environmental effects for the chemicals of concern

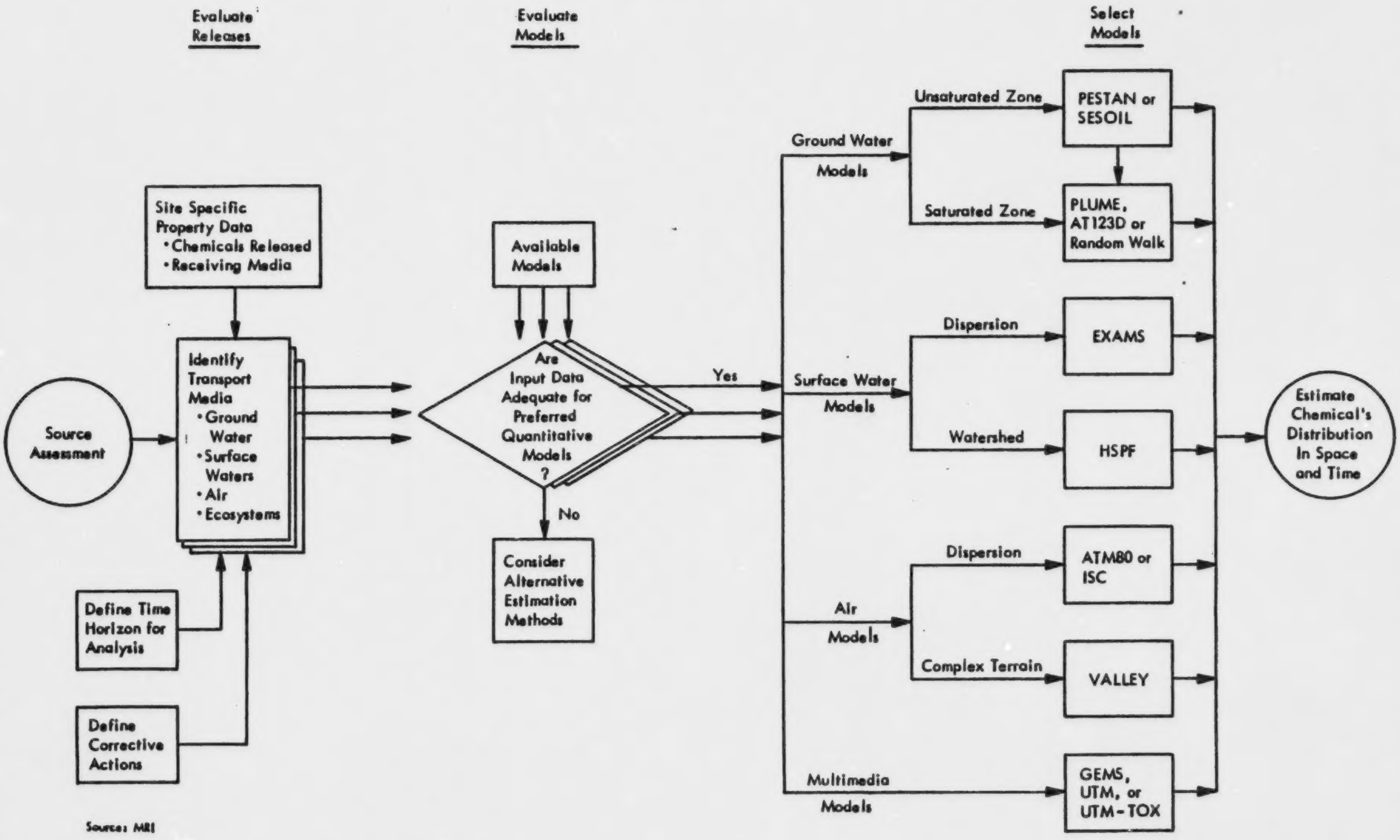
- Identify ranges of responses known, and especially those that could occur at predicted environmental exposures

- Select or develop chemical-specific dose-response relationships for effects of concern

- Develop (through selected extrapolation methods) risk factors for specific predicted environmental doses

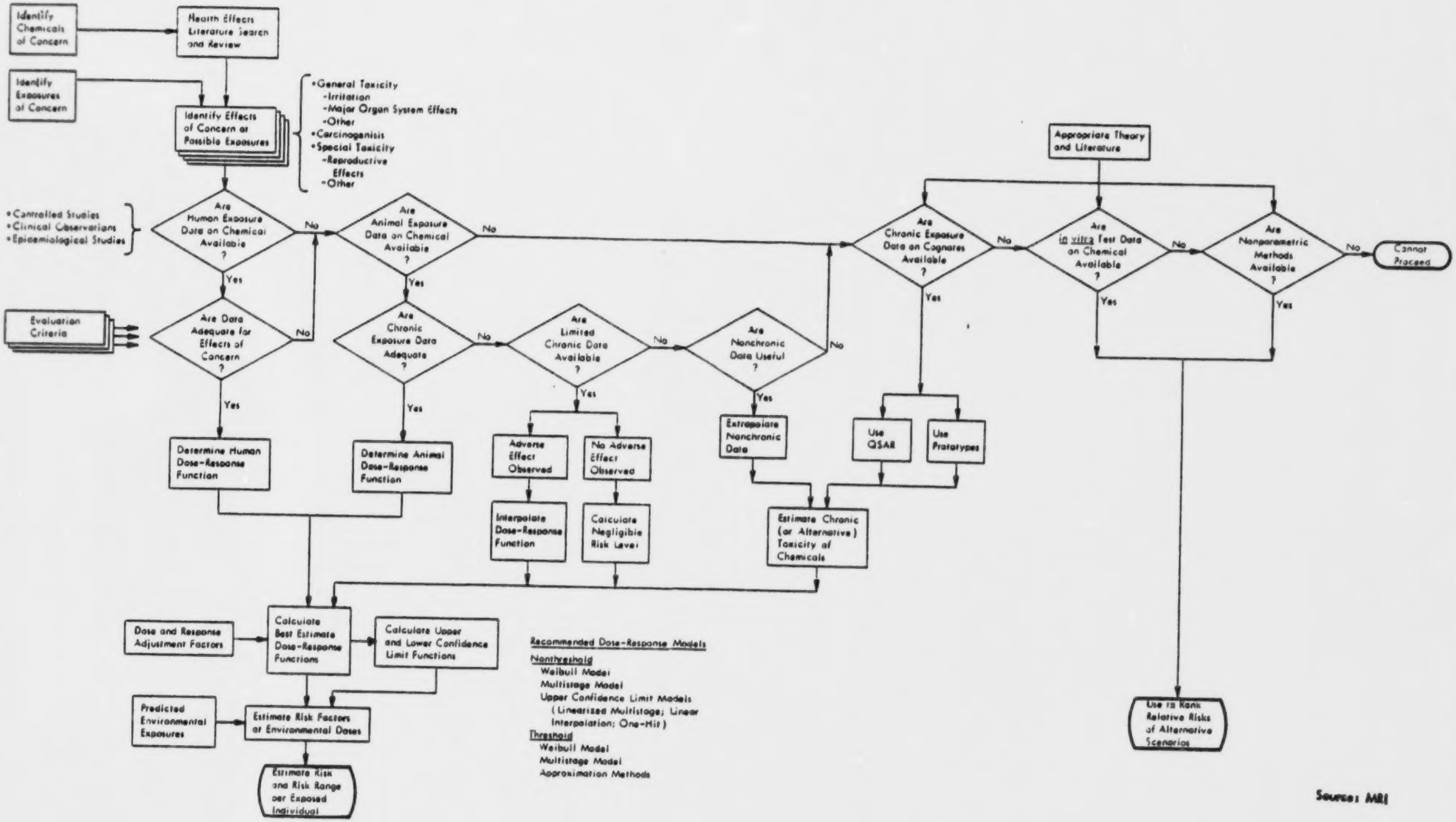
A schema for selection of health effects estimation models, depending on the availability of data is shown in Figure S-5.

The preferred dose-response model depends on the type of effect, the quality of the available data, and whether one is calculating a maximum likelihood estimate (MLE) or an upper (or lower) confidence limit. For effects that are believed not to have a threshold dose (such as cancer), the nonthreshold Weibull model is generally recommended for obtaining best point estimates, but the multistage model may be preferred with some data sets. The linearized multistage model is recommended for calculating the upper confidence limits, since it has been widely used for this purpose already by EPA. For seriously deficient data sets, the linear interpolation method or the one-hit model can be used to estimate upper confidence limits. For effects believed to have a threshold dose, the threshold version of the Weibull model is generally recommended for best point estimates above the threshold, but again the multistage model may be preferred with some data sets. Estimation methods are provided for determining the threshold dose from established acceptable daily intakes or threshold limit values and from experimentally determined no observed effect levels, or lowest observed effect levels.


Evaluate Releases
Evaluate Models
Select Models
Source Assessment
Site Specific Property Data
• Chemicals Released
• Receiving Media
Identify Transport Media
• Ground Water
• Surface Waters
• Air
• Ecosystems
Define Time Horizon for Analysis
Define Corrective Actions
Available Models
Are Input Data Adequate for Preferred Quantitative Models ?
Yes
No
Consider Alternative Estimation Methods
Ground Water Models
Unsaturated Zone
Saturated Zone
PESTAN or SESOIL
PLUME, AT123D or Random Walk
Surface Water Models
Dispersion
Watershed
EXAMS
HSPF
Air Models
Dispersion
Complex Terrain
ATM80 or ISC
VALLEY
Multimedia Models
GEMS, UTM, or UTM-TOX
Estimate Chemical's Distribution In Space and Time

Source: MRI

Figure S-4 - Schema for Selecting of Models for Analysis of Transport and Fate of Pollutants Entering the Environment


Identify Chemicals of Concern
Health Effects Literature Search and Review
Identify Exposures of Concern
Identify Effects of Concern at Possible Exposures
•General Toxicity
-Irritation
-Major Organ System Effects
-Other
•Carcinogenisis
•Special Toxicity
-Reproductive Effects
-Other
•Controlled Studies
•Clinical Observations
•Epidemiological Studies
Are Human Exposure Data on Chemical Available ?
Yes
No
Evaluation Criteria
Are Data Adequate for Effects of Concern ?
Yes
No
Determine Human Dose-Response Function
Are Animal Exposure Data on Chemical Available ?
Yes
No
Are Chronic Exposure Data Adequate ?
Yes
No
Determine Animal Dose-Response Function
Are Limited Chronic Data Available ?
Yes
No
Adverse Effect Observed
No Adverse Effect Observed
Interpolate Dose-Response Function
Calculate Negligible Risk Level
Are Nonchronic Data Useful ?
Yes
No
Extrapolate Nonchronic Data
Estimate Chronic (or Alternative) Toxicity of Chemicals
Appropriate Theory and Literature
Are Chronic Exposure Data on Cognates Available ?
Yes
No
Use QSAR
Use Prototypes
Are in vitro Test Data on Chemical Available ?
Yes
No
Are Nonparametric Methods Available ?
Yes
No
Cannot Proceed
Use to Rank Relative Risks of Alternative Scenarios
Dose and Response Adjustment Factors
Calculate Best Estimate Dose-Response Functions
Calculate Upper and Lower Confidence Limit Functions
Predicted Environmental Exposures
Estimate Risk Factors at Environmental Doses
Estimate Risk and Risk Range per Exposed Individual
Recommended Dose-Response Models
Nonthreshold
Weibull Model
Multistage Model
Upper Confidence Limit Models
(Linearized Multistage; Linear Interpolation; One-Hit)
Threshold
Weibull Model
Multistage Model
Approximation Methods

Source: MRI

Figure S-5 - Schema for Selection of Health Effects Estimation Models Depending on Availability of Data

5. Adverse impact estimation and summation is an integrative step that involves estimation of the probabilities and extents of adverse health and environmental effects actually expected from the predicted exposures, including:

- Apply dose-response functions to exposed individuals by exposure group
- Identify any especially sensitive subpopulations of concern
- Make best estimates of the risks for each effect in each subpopulation
- Make best estimates of the total number of cases of each effect
- Estimate the uncertainty range for each best estimate

6. Uncertainty analysis considers both systematic and random sources of errors in all elements of the risk assessment process, including:

- Identify uncertainties for each factor contributing to risk for each option assessed
- Perform sensitivity analyses of key variables
- Estimate uncertainties of all factors
- State uncertainties with same confidence bounds for all factors
- Aggregate uncertainties across entire assessment for each option
- Compare total uncertainties for all options and also relative uncertainties if a particular factor is common across options
- State the risk range for each option as a best estimate of risk, R, times an order of magnitude factor $10^{\pm U}$, where U reflects the aggregated total or relative uncertainty

7. Reporting and communication of the results and conclusions requires careful planning to obtain maximum value from the risk assessment. The report should:

- Provide sufficient detail on the technology, wastes, and waste management alternatives being assessed for clarity
- State clearly the modeling techniques employed, data sources used, and all assumptions made
- Show and compare consistently best estimates of health risks and their uncertainty ranges for all alternatives assessed

- Provide similar best estimates and uncertainties, if appropriate for ecological or other environmental risks, costs of control technologies, and other socioeconomic costs, risks, and benefits for alternatives assessed

- Prepare extended (e.g., 10 page) and concise (e.g., one page) summaries of the assessment and its results and conclusions

- Make oral presentations as appropriate

- Make special effort to place the risks, costs, and benefits of the alternatives into perspectives helpful to the reader, audience, and decision maker as appropriate

The results should be summarized in a concise form with sufficient clarity to be useful to decision makers who are not technical experts, but should be supported by enough technical detail to permit analysis of the procedures used and assumptions required.

Conclusions

Important features of the methodology are:

- It is designed to assess the consequences of disposing of specific wastes with specific technologies at specific sites, through the use of carefully constructed scenarios and actual or estimated technological, meteorological, hydrogeological, environmental, toxicological, and demographic data.

- It provides a modular framework for a series of steps, most of which must be performed in given assessments. This modular nature permits one to respond to differences in availability and applicability of data or analytical techniques, and to incorporate refinements or extensions of a presently proposed technique, alternative techniques, or new techniques as they become available.

- It contains procedures for selecting among available analytical techniques for each step so that maximum use can be made of the data available.

- It analyzes uncertainties in all steps and aggregates them across all steps in each assessment.

The methodology is oriented throughout to the development of "best" estimates (often maximum likelihood estimates, MLEs) for each factor rather than "worst case" or "worst credible case" estimates. The best estimates for the contributing factors are combined to provide a best estimate for each kind of effect. The analysis does not inconsistently mix best estimates (or MLEs) for some factors with upper confidence limit estimates (e.g., 95%) for other factors. (The result of such a combination would be an estimate of overall effect at some ill-defined point between an MLE and a worst case.)

The analysis does address confidence limits in the uncertainty analysis, and both the best estimate and the uncertainty range can be provided to the decision maker. Analysis of uncertainties considers both systematic and random sources of error. Uncertainties are estimated for each factor contributing to the risk for each option assessed, and then stated with the same confidence bounds for all factors.* The uncertainties are aggregated across the entire assessment for each option and risk ranges for options are compared.

The methodology focuses on public health impacts of hazardous wastes. Ecological and socioeconomic impacts are considered only briefly, but should be assessed in greater detail than indicated herein for many decisions. The methodology would require substantial input data and resources to yield quantitative point estimates and uncertainty bounds for risks, but the results should provide a better basis for most decision making than unrealistic, overly conservative or overly optimistic estimates. Further research is needed to demonstrate the methodology's reliability and its usefulness in hazardous waste management decisions.

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*The uncertainty for each factor can be stated to within one standard deviation ($\pm 1\ \sigma$) of the best estimate or some higher confidence interval such as $2\ \sigma$ or $3\ \sigma$. The larger intervals after aggregation will tend to increase the overlap of risk estimates for the options being compared, and the choice of interval probably will not make a big difference in most decisions between technologies.

I. INTRODUCTION

Decision making in the public interest requires consideration of the range of consequences -- benefits, costs, and risks to individuals, groups, business, and the environment -- posed by alternative technological choices. Legislation often requires that government agencies and industry reduce risks to human health and the environment to "reasonable" levels. Executive Order 12291 directs federal agencies to prepare Regulatory Impact Analyses (RIAs) that describe the benefits and costs to society for proposed major regulations. A major policy issue confronting regulatory agencies is how best to choose among multiple regulatory and nonregulatory approaches in managing our diverse technologies when the magnitudes of the consequences are uncertain. Decisions are particularly difficult when the risks are highly uncertain but possibly quite large. Many studies have, therefore, been initiated by government agencies and the research community to develop better ways of estimating technological risks and of using the results in controlling these risks at acceptable levels.

This study was initiated at Midwest Research Institute (MRI) by the U.S. Environmental Protection Agency (EPA) in support of EPA's needs to assess the risks and impacts of regulatory decisions involving hazardous wastes.

A. Risk Assessment Role in Decision Making

Recent studies by committees of the National Research Council, a study group of the Royal Society, and by others have concluded that the science-based parts of the risk assessment process should be as independent as possible of the ultimate decision-making steps, although the latter obviously should draw extensively on the former (see NRC/NAS, 1982; NRC/NAS, 1983; and Royal Society, 1983). Bills introduced in recent U.S. Congresses (e.g., the "Risk Assessment Research and Demonstration Act of 1985") also reflect a conclusion that information on the risks of a given choice should be compared with the risks of other practical choices and with other everyday risks, so that the decision makers and the public can gain a useful perspective of the risks, costs, and benefits of the available options (U.S. Congress, 1985). Another lesson from recent study is that the uncertainties in estimating the risks should be made explicit. A statement of estimated adverse health effects should identify not just a single-valued prediction, but a range of reasonably probable forecasts. The decision maker can then compare the ranges as well as the point estimates.

Recent research has also shown a need to reevaluate the role of "conservatism" in assessing and managing risk. Making a "conservative decision" (i.e., one that is likely to be more protective of health and the environment than an alternative decision) is widely accepted as a prudent practice in risk management. In keeping with the recommended separation of risk assessment and risk management activities, however, conservative assumptions, conservative models, conservative estimates, etc., should not be key elements in the science-based risk estimation steps. A catenation of conservative assumptions, models and estimates throughout a risk assessment can lead to a "worst-case" (or even worst-of-the-worst-cases) prediction that may be of little value (or possibly misleading) to the decision maker. For this reason, the concept of "worst-credible case" has received some emphasis recently.*

Most decisions on hazardous waste sites actually involve "either-or" choices between technological alternatives with different risk levels rather than a "yes-no" choice on a single risk. When dissimilar alternatives require different analysis procedures, conservatism ambiguously or inconsistently applied could lead to biased results and poor decisions -- even to the choice of a technology that is less protective of human health and the environment and possibly more costly to society than an available alternative. Best estimates of the risks, costs, and benefits for the alternatives, coupled with consideration of their uncertainties (including worst-credible case considerations), should produce the optimal basis for decision making. The Council on Environmental Quality has recently noted that "rules of reason" should replace worst case analysis as the basis of regulatory decision making (CEQ, 1985). The Council has also noted the need to and the difficulty of making environmental regulations in the face of incomplete or unavailable information, and has made suggestions (CEQ, 1986).

B. Risk Assessment Needs Under RCRA and Superfund

The Resource Conservation and Recovery Act (RCRA) of 1976 and Hazardous and Solid Waste Amendments (HSWA) of 1984 are major legislation controlling hazardous waste disposal. Under RCRA, EPA designates specific chemicals and specific industrial waste streams as hazardous and regulates their treatment, storage, and disposal. RCRA and HSWA are less specific about the need to determine the reasonableness of risks or to perform risk assessments than are some other environmental and consumer protection laws, such as the Toxic Substances Control Act, the Federal Insecticide Fungicide and Rodenticide Act, and the Consumer Product Safety Act. Nevertheless the RCRA language clearly implies that risks will need to be studied in some cases.

For example, RCRA defines hazardous waste as "a solid or combination of solid wastes which, because of its quantity, concentration or physical, chemical or infectious characteristics may: (a) cause or significantly contribute to an increase in mortality or to an increase in serious irreversible or incapacitating reversible illness; or (b) pose a substantial present or potential hazard** to human health or the environment when improperly treated, stored, transported, disposed of, or otherwise mismanaged."

Sec. 3013 of RCRA, "Monitoring, Analysis, and Testing," addresses the issue of risk indirectly. It states that upon receiving information that the presence or release of hazardous waste at a treatment, storage, or disposal facility (TSDF) may present a substantial hazard to human health or the environment, the EPA Administrator can require that the owner/operator of the site conduct monitoring, testing and analysis to determine the nature and extent of such hazard.

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* Efforts to define worst-credible cases can also be controversial; the courts have had to grapple with this issue.

** RCRA does not define 'hazard,' but as used here to define 'hazardous waste' it appears to be essentially synonomous with conventional definitions of 'risk.'

Sec. 3019, "Exposure Information and Health Assessments" (added in the 1984 amendments), speaks most directly to risk assessment needs. It identifies the kinds of information related to potential human exposure to environmental contaminants that an owner/operator of a hazardous waste TSDF must submit to EPA before a permit to operate is granted. It provides procedures for determining if health assessments are needed, for establishing priorities among such needs, and for initiating such assessments. It also defines the general contents of health assessments to include evaluation of risks to potentially affected populations.

The HSWA directed a phase-out by 1990 of previously used land filling or other land disposal of hazardous waste, and increased interest in searching for and demonstrating alternative disposal methods that posed less environmental risk. HSWA also provided for controlling environmental contamination from underground storage tanks.

The Comprehensive Environmental Response, Compensation and Liability Act (CERCLA or Superfund) of 1980 and the Superfund Amendments and Reauthorization Act (SARA) of 1986 provided for the evaluation and management of existing hazardous waste sites and spills of hazardous substances into the environment. Under Superfund, EPA has placed some 950 sites on the National Priority List, based on a hazard ranking systems. Remedial investigation/feasibility studies (RI/FS) are first initiated followed if appropriate by remedial designs and remedial actions. Remediation at a site is undertaken by private sector principal responsible parties (PRPs), if they can be identified, or by the U.S. Army Corps of Engineers (with resources from the industry-supported Superfund) if they cannot. In either case, risk assessment and risk-cost-benefit assessment have become an important part of the RI/FS to determine the extent of remediation needed and of the remedial design, where competing demands for environmental risk reduction and allocation of limited resources often must be compared and balanced before reaching decisions.

Superfund also provided for EPA to establish reportable quantities (RQs) for lists of hazardous chemicals posing "substantial danger to the public health or welfare or the environment." Releases of listed substances in amounts greater than their RQs triggers notification requirements. Establishment of RQs (over 600 substances to date, with values of 1, 10, 100, 1,000, etc., pounds) have incorporated consideration of health and environmental risk.

C. Study Objectives, Origins, and Scope

The commitment of EPA to using risk assessment effectively in making consistent regulatory decisions in all of its program areas has been expressed by present and previous EPA Administrators and is described in a 1984 report to the public (EPA, 1984). EPA continues to examine ways to improve the risk assessment and risk management processes. The present study concerns EPA needs in a very important problem area--hazardous waste disposal.

1. Objectives: The overall goals of this project were to explore and recommend risk assessment methodologies for use in decisions involving hazardous waste regulations. Specific objectives were: to evaluate currently available techniques and models that might be used for various steps in this methodology; to identify the most generally applicable and efficient methods for each step; and to recommend a general approach based on selected methods.

2. Origins: This study began in late 1982 when EPA was preparing for several decisions under RCRA about regulating the management of hazardous wastes. EPA's Office of Solid Waste (OSW) was considering alternative regulatory approaches, such as prohibition of land disposal for certain hazardous wastes, and was evaluating potential impacts of these alternatives on human health, the environment, the economy, and specific industries. In cooperation with OSW, OPPE initiated studies with MRI directed toward a methodology for quantitative assessment of potential risks to human health from the use of various technologies for the treatment, storage, and disposal of hazardous wastes.

The study first reviewed, evaluated, and compared reported methods for predicting the environmental transport of pollutants released from a hazardous waste treatment, storage, or disposal facility and for estimating human health effects from environmental exposure to such pollutants. Methods that appeared to be most applicable with the kinds and quality of information and data usually available were selected for further consideration and possible integration into a general approach that could be applied broadly, rapidly, and quantitatively to many wastes and many waste disposal alternatives. The study then considered other factors: alternative treatment and disposal technologies, transportation risks, occupational exposures, release rate parameters, corrective actions, costs, and environmental impacts. The quantitative estimation of public health effects from environmental exposures, however, remained the focal point of the study. Comments from many reviewers of interim manuscripts and a draft report (MRI, 1983) led to several improvements in the methodology.

The methodology was then applied in pilot analyses of three representative wastes, which required further development of the overall methodology. An interim report was prepared (MRI, 1984a). Review comments were again incorporated in a draft report summarizing the methodology and results of the pilot studies (MRI, 1984b). This draft was made available to interested researchers and the public for comment. The Environmental Engineering Committee, EPA's Science Advisory Board also reviewed this report, discussed the methodology and results with the OPPE-MRI project team, and issued a review (SAB, 1985). Our evaluation and development of risk assessment techniques benefited from these extensive reviews and suggestions.

3. Scope: The scope of this study had three major tasks: (1) an overview of the risk assessment process (including necessary definitions) and of the components of risk assessment for hazardous wastes disposal; (2) reviews of methods for specific steps in hazardous waste risk assessment including source assessment, analysis of environmental transport and fate, exposure prediction, analysis of health effects and prediction, assessment of environmental and other impacts, impact integration, and uncertainty analysis; and (3) development of a general approach for assessing risks in hazardous waste management.

Our study was constrained in scope by available resources. Several assumptions and limitations were made, the most significant of which are noted here, because they may require further consideration in other specific risk assessment applications.

- A solid waste was defined as hazardous if it is listed in the appropriate section of the Code of Federal Regulations or exhibits a significant degree of ignitability, corrosivity, reactivity or toxicity.
- The risk assessment approach should be oriented toward RCRA-related decisions concerning hazardous waste disposal.
- The approach should be applicable to specific hazardous waste treatment, storage and disposal facilities (TSDFs) or to specified hazardous wastes.
- The approach should be applicable to multiple technologies, including: landfills; surface impoundments; surface spreading; storage in piles or containers; deep well injection; chemical and biological treatments; incineration on land or at sea; and combustion in boilers.
- The approach should be applicable to existing sites containing hazardous wastes, existing TSDFs, and proposed new central or dispersed facilities.
- The approach should be applicable to a range of potential regulatory decisions, such as: exclusion or acceptance of designated wastes (e.g., from a landfill or incinerator); promulgation of specifications or standards for given disposal technologies (e.g., liners for landfills, or control of emissions and effluents); and acceptance or rejection of designated sites for stated activities (e.g., based on waste characteristics and amounts, hydrogeological and meteorological conditions, human population distribution and other environmental factors).
- The approach need not be oriented now to making waste management decisions on a national level on specific wastes or waste sources. National considerations will be taken into account as needed in future decisions.

- The approach should address all releases of pollutants from TSDFs to air and water that may affect the public. However, releases from transportation of hazardous wastes are noted only briefly. They may need to be considered at length in many real-life decisions.

- The approach should take a long-term multimedia view of environmental transport of pollutants from points of release to points of exposure of human or nonhuman receptors.

- The approach should focus on the potential human health effects of toxic pollutants. It should address primarily the health risks of the general population in the vicinity of the TSDF. The public is assumed not to have access to the site. Occupational exposures at the TSDF are noted only briefly; they may require further consideration in some decisions.

- Methods for assessing impacts on the physical and ecological environment are examined only briefly. Impacts on such factors as the atmosphere and the flora and fauna may require detailed evaluation in some decisions.

- The study notes only very briefly socioeconomic impacts. Such factors as benefit-cost ratios, equity considerations, land-use planning and social acceptability of alternatives may require in-depth consideration in some decisions.

References to Chapter I

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U.S. Congress, "Risk Assessment Research and Demonstration Act of 1985." Bill H.R.2749. Introduced in 99th Congress by Congressman Donald Ritter and others. June 12, 1985. 13 pp.

II. RISK ASSESSMENT AND RISK MANAGEMENT

Systematic assessment of the risks to human health and safety and to environmental values has become a formal activity for regulatory purposes only within the past few decades. Neither the definitions of risk assessment/management terms nor the scopes of the processes are standardized yet. The following sections describe first the terminology used in this report, and then a useful framework for assessing and managing risks of hazardous waste disposal.

A. Terminology

Risk assessment/management concepts developed independently in diverse fields with substantially distinct literatures and differing terminologies. The risk-related literature has grown rapidly in the past decade or so, and interactions between researchers in different fields have increased, but a generally accepted, standardized nomenclature is still unavailable. We have carefully reviewed the terminology in use in the literature and have selected a composite set of definitions for our work, as described in Appendix A and summarized in the two subsections following.

1. Recent usage: Numerous authors have defined risk-related terms, but they have seldom agreed with each other and have at times been inconsistent or confusing within their own usage. A review and bibliography of recent usage in the literature is provided in Appendix A. Overall, the literature reveals that risk assessment is an immature discipline without the kind of standardized nomenclature one finds in an older discipline such as one of the physical, biological, or social sciences.

Several recent publications have attempted to define terms, but none can be regarded as the final word. In short, the terminology is still evolving. It lacks consistency, even for such basic terms as "risk," "risk assessment," and "risk management."

Some authors feel that "risk" must be a quantitative expression of probability, while others do not; a few equate risk with "uncertainty," others with "hazard." Some define "hazard" as intrinsic toxicity, others as a situation that could lead to harm, and still others as a dangerous technology. "Analysis" and "assessment" are used interchangeably by some authors, but not by others.* Particularly troublesome have been the inconsistency and the varying interrelationships shown for such terms as: identification, estimation, determination, characterization, evaluation, analysis, assessment, and management. For example: "estimation" is called "characterization"; "evaluation" is used in several ways; and "management" is often limited to "reaching a decision." One recent author classified "risk analysis" as a subset of cost-benefit analysis, while another curiously subsumed risk assessment and management under "analysis."

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* According to dictionary definitions, "analysis" (from 'to dissolve') implies separation of a whole into its component parts, followed by identification and quantification of the parts. "Assessment" (meaning 'to assist the office of judge') implies appraisal, valuation, judgment, and a summing up. The journal of the Society for Risk Analysis uses the terms interchangeably.

Different agencies of government and different committees of the National Research Council, National Academy of Sciences, have used substantially differing terms and definitions. An illustration of the diversity that exists among authors on basic terms is seen in Table II-1. In addition, the overall process of studying and managing technological risks tends naturally to have several sequential steps; many analysts tend to define a given step to include all prior steps in the sequence. Thus, source assessment and environmental transport analysis can become subsets of exposure assessment, and all three can become subsets of risk assessment. Risk assessment is occasionally described as a component of risk management.

Based on our review of terminology used in the literature, an attempt was made to develop a set of terms that are internally consistent and widely acceptable, as discussed in the next subsection.

2. Definitions adopted: We applied two guidelines in the development of definitions:

- The terminology should reflect as well as possible the best usage in the recent literature, both in the United States and internationally.

- The terminology should be self-consistent across the whole process of assessing and managing risks, including those elements involving judging the safety and acceptability of risks, making regulatory decisions, and implementing risk controls as appropriate.

Particular attention was given to terminology used in the Stallones' committee report, Risk Management in the Federal Government: Managing the Process (NRC/NAS, 1983), because this terminology was well received by the EPA (EPA, 1984). It is not, however, without problems, and many authors have made efforts to improve upon it (Table II-1), including a prestigious task force of the Department of Health and Human Services (USDHHS, 1986) (see also Appendix A). The NRC/NAS terminology will undoubtedly be supplanted in the future.

The relationships defined below provide a background for the more complex relationships in the framework for assessing and managing risks described in the next section.

TABLE II-1

EXAMPLES OF DIVERSE TERMINOLOGY IN RISK ASSESSMENT LITERATURE

Reference	Comprehensive Risk Terms	Principal Components	Subterms
Otway & Pahner, 1976	Assessment	Estimation Evaluation	
Rowe, 1977; 1983	Assessment	Determination	{Identification Estimation
		Evaluation	{Aversion Acceptance
Kates, 1978; Whyte & Burton, 1980	Assessment	Identification Estimation Evaluation	
Somers, 1979	Management	Hazard identification Risk estimation Risk evaluation	
Conrad, 1980; Greer-Wootten, 1980; Cullingford et al., 1982	Assessment	Analysis (or estimation) Evaluation Management	
Gusman et al., 1980	Assessment	Exposure assessment	{Magnitude Probability
		Dosage (hazard) assessment	{Adverse effect Probability
NRC/NAS, 1980	Assessment	Exposure analysis Pathological activity or hazard appraisal Combination of exposure and hazard estimates	
Porter et al., 1980	Assessment (equated with risk/benefit analysis)		

TABLE II-1 (Continued)

Reference	Comprehensive Risk Terms	Principal Components	Subterms
Conway, 1982	Assessment	Analysis (evaluation of scientific data) Evaluation of socio-econo-political factors	
NRC/NAS, 1982	Analysis	Assessment Evaluation	
NRC/NAS, 1983	Assessment	Hazard identification Dose-response assessment Exposure assessment Risk characterization	
CRS, 1983	Assessment/ analysis	Source assessment Pathway-to-man assessment Impact assessment	
Royal Society, 1983	Assessment	Estimation	Identification of outcomes Estimation of magnitude of consequences Estimation of probabilities of outcome Determine significance
		Evaluation	Study trade-offs of perceived risks and benefits
DSMC, 1983	Analysis	Assessment	Identification of cost, schedule, or performance goal Estimation of probability of achieving goal
		Reduction Management	
Davies, 1984	Assessment	Estimation of probability of hazard occurrence Determination of types of hazards posed	

TABLE II-1 (Continued)

Reference	Comprehensive Risk Terms	Principal Components	Subterms
Davis, 1984 (continued)	Assessment (continued)	Estimation of number of people exposed and number incurring adverse effects	
	Management	Acceptability judgment Action selection Implementation Evaluation of results	
	Control	Priority setting Assessment Management	
Moghissi, 1984	Analysis	Assessment	Engineering failure assessment Exposure assessment Effects assessment Risk characterization Assessment policy
		Management	Risk value Uncertainty-of-risk value Cost impact Cost/benefit analysis Perceptions, constraints, intangibles
Park & Snee, 1984	Assessment	Hazard identification Hazard evaluation Risk evaluation	
	Management (or regulatory response)	Evaluation of benefits *versus* risks, costs, and alternatives	
Smith, 1984	Assessment	Hazard identification Hazard evaluation Exposure identification Exposure evaluation	

TABLE II-1 (Continued)

Reference	Comprehensive Risk Terms	Principal Components	Subterms
USNRC, 1984 and 1986	Probabilistic risk assessment	Systems analysis Fault tree/event tree analysis Human factor analysis Accident precursor analysis Accident sequence analysis Containment analysis	
USNRC, 1985	Risk management	Accident prevention Accident management Consequence mitigation	
OSTP, 1985	Assessment	Hazard (toxicity) assessment Exposure assessment	
Ricci et al., 1985	Assessment	Hazard Context Consequences Uncertainty Severity Magnitude	
Bailar & Thomas, 1985	Analysis	Study	Hazard identification Risk assessment (development of conditional probabilities) Risk-benefit analysis
		Interpretation	Risk appraisal Translation (into relevant terms of political theory, law, economics, and human behavior)

TABLE II-1 (Continued)

Reference	Comprehensive Risk Terms	Principal Components	Subterms
Morgan, 1985	Assessment	Exposure processes Effects processes Perception processes Evaluation processes	
	Management	Strategy identification Acceptable/optimal risk determination Risk abatement	
Skinner & Miller, 1985	Assessment	Hazard identification Risk estimation Risk evaluation (including management)	
Travis, 1985	Analysis	Exposure assessment	Pathway Identification Quantification of concentrations in space and time Target populations
		Effects assessment	
		Hazard assessment	Structure/activity models Experimental studies Epidemiological studies
Neal, 1985	Characterization	Exposure assessment	Concentrations Duration
		Risk estimation	Quantification
	Management	Policy judgments	Human health considerations Economic factors Political considerations
Boykin, 1985	Analysis	Risk assessment	Hazard assessment (risk identification) Exposure estimation Risk characterization (quantification and uncertainty analysis)
		Risk management	Risk evaluation Technical feasibility of control Social, economic, political factors Decisions

TABLE II-1 (Concluded)

Reference	Comprehensive Risk Terms	Principal Components	Subterms
USDHHS, 1986	Assessment	Hazard identification	Qualitative or quantitative determination of potential hazard from a condition or substance
		Hazard characterization	Characterize action of hazard Dose-response assessment Determine differences in risk across subpopulations
		Exposure characterization	Qualitative and quantitative evaluation of likely exposure
		Risk determination	Integration Binary (risk/no risk) conclusions Quantitative multidimensional conclusions (including sensitivity testing and uncertainty characterization)
Hallenbeck & Cunningham, 1986	Assessment	Exposure characterization	
		Health effects characterization	Qualitative evaluations Quantitative evaluations
		Risk analysis	Individual excess risk Number excess cases Sensitivity analysis
		Acceptable concentration calculation	
Smith et al., 1988	Assessment	Hazard identification	
		Hazard accounting (defining the system)	
		Environmental pathway evaluation	
		Risk characterization (human health and ecosystem)	
		Risk management	

An action or combination of actions (events, conditions, challenges, decisions, or causes) produces one or more consequences (outcomes, responses, impacts, or effects). These consequences are judged to be beneficial (favorable, advantageous, propitious or good), adverse (detrimental, harmful, injurious, or bad), or neutral, depending on the value system of the party or parties doing the judging.* A potential consequence deemed to be adverse is viewed as a threat.** An action or condition posing a threat is a hazard, i.e., a hazard is a potential source of adverse impacts, or in popular terminology, a source of risk.*** This study focuses on adverse impacts on human health and safety and on the environment from hazardous chemicals. The degree of hazard of a chemical depends on how much is present, its potential for release to the environment, its intrinsic toxicity, and its physicochemical properties.

Risk (noun) is an expression of the uncertain potential of incurring a specified adverse consequence (e.g., death) during some stated measure of interval, e.g., time, million miles, hundred skydives, etc. All expressions of risk are conditional. Risk may be usefully expressed either quantitatively or qualitatively:

- A quantitative statement of the probability of occurrence of a defined adverse effect, based on adequate amounts of the required kinds of information and data. A statement of risk as a probability has meaning only if one states the units of measure and the conditions applicable. (Note: A definition of risk as probability multiplied by the magnitude of the consequence (i.e., the expected value) is also widely used in the literature.)

- A qualitative statement of the likelihood or possibility of occurrence of one or more identified adverse effects, based on partial or minimal information or historical perspective.

In many cases of regulatory interest a sequence of several steps (actions and their consequences) may be involved between the initial source and ultimate consequences of concern, such as actual effects on human health. For environmentally related risks, a designated location, activity or use from which a toxic substance enters this sequence may be considered as a hazard. Exposure is said to occur at the point in the sequence at which the toxic substance is present at the interface between the environment and the biological organism. The environmental dose is the amount of the substance that actually contacts or enters the organism through bodily membranes and portals: intact or broken skin, eyes, nose, and mouth.* Subsequent steps within the organism may be involved before the specified effect occurs. The risk for this effect is then estimated by appropriate calculation based on the chemicals, steps and conditions involved and assumptions required (as will be discussed later).

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* A consequence deemed beneficial by one person or group may be deemed of no value or adverse by another (or even by the same person at another time), e.g., a "snail darter," a zero sum game, an election result, or a suicide. Values thus enter into the study of risks at the earliest stage, and enter subsequently in many ways, either explicitly or subtly. Adverse health effects should generally be objectively definable.

** "Potential" means "could occur in the future."

***A committee of the National Research Council stated that the hazard of a chemical is a function of both its intrinsic toxicity and use pattern (NRC, 1975). Saxena and Fisher (1981) use the term "hazard assessment" to include many of the areas covered herein by risk assessment.

"Exposure assessment" is often used to describe different sets of activities by researchers with different viewpoints. Some researchers consider exposure assessment to begin with chemical analysis of the contaminants in the air, water, food, surfaces, etc., which people actually inhale, ingest, touch, etc. By knowing concentrations and assuming the daily volume of air breathed, tapwater consumed, etc., these researchers estimate the exposure rate and exposure dose over a given duration for each exposed individual. The exposure assessment is usually completed by quantifying the known or assumed population at risk. Other researchers, however, may place greater emphasis in exposure assessment on analyzing or modeling the transport and interactions of chemical substances from the point at which they enter the environment through air, water, land, and ecosystems until they reach receptor populations, i.e., they quantify the points in space and time that toxicants and populations intercept each other, as well as predict the extents of exposures that could result. Still other researchers may begin the exposure assessment with qualitative and quantitative analyses of the entry of contaminants into the environment, i.e., with an assessment of the sources. Thus, Hushon and Clerman (1981) divided exposure assessment into five steps: chemical description; materials balance; pathways of environmental release; population profiles; and "assessment" in which the environmental concentrations and population profiles are combined to give exposure profiles. In one recent report (OTA, 1984), the exposure assessment was extended to include absorption and transport within the organism to the site of toxic activity. Many additional factors can affect biological uptake of a given chemical, including the presence of other chemicals.

In the present research, the terms "source assessment," "environmental transport and fate analysis," and "exposure prediction" are used for clarity instead of the less definitive "exposure assessment" terminology.

We adopt "risk assessment" to describe a broad study process** consisting of several analytical components. The nature of specific analytical components varies with a given risk assessment problem, but generally includes: identification and characterization of sources of potential threats (i.e., hazards); identification and quantification of processes by which potential receptors are exposed; identification and quantification of populations at risk; development of predictive cause/effect relationships from available data; combination of data on exposure levels, cause/effect relationships, and populations at risk to estimate the probabilities of adverse effect on exposed individuals or populations. The results of a risk assessment are sometimes expressed as estimated probabilities of impacts per average or most exposed individual, or as integrated estimates of the total impacts on an exposed population. In either case, the results should provide not only the point estimates but also the ranges of uncertainty for each estimate. A risk study to this point consists of an analysis--in as scientifically defensible, value-free* a manner as possible--of several elements associated with potential adverse effects of a situation. Variations of the risk assessment process can be made, for example, to yield estimates of maximum exposure levels or source strengths that can be permitted while achieving a stated acceptable risk level.

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* Environmental dose as defined here is analogous to the administered dose in a controlled toxicological study.

** The terms "risk analysis" and "risk evaluation," which have been defined many ways in the literature, are not used. Neither of these terms are included in EPA's new "Glossary of Environmental Terms," but "risk assessment" is included (EPA, 1988).

B. Framework for Assessing and Managing Risks

The making and implementing of decisions to control risks requires much more information than the estimates of their magnitude. It usually requires objective estimates and comparison of the costs and benefits of available alternatives, i.e., comparative risk-cost-benefit assessment**, information on public perceptions of the risk and on feasibility of implementing various management strategies is also usually considered. MRI's view of an overall framework for assessing and managing technological risk is outlined in Figure II-1. The health and environmental risk assessment, an important part in the overall process, is shown with seven components as developed in this study for hazardous wastes: (1) source (hazard) assessment; (2) transport and fate analysis; (3) exposure prediction; (4) health and environmental effects analysis; (5) adverse impact estimation integration; (6) uncertainty analysis; and (7) report and compare the results as necessary. Some of these components would differ in assessing the risks of other technologies.

Important aspects of comparative risk-cost-benefit assessment and risk management are discussed briefly below.

1. Comparative risk-cost-benefit assessment: Comparative risk-cost-benefit assessment is a science-based description and comparison of the estimated or forecasted risk, costs, and benefits of a policy, course of action, or technological or siting alternative. It can include:

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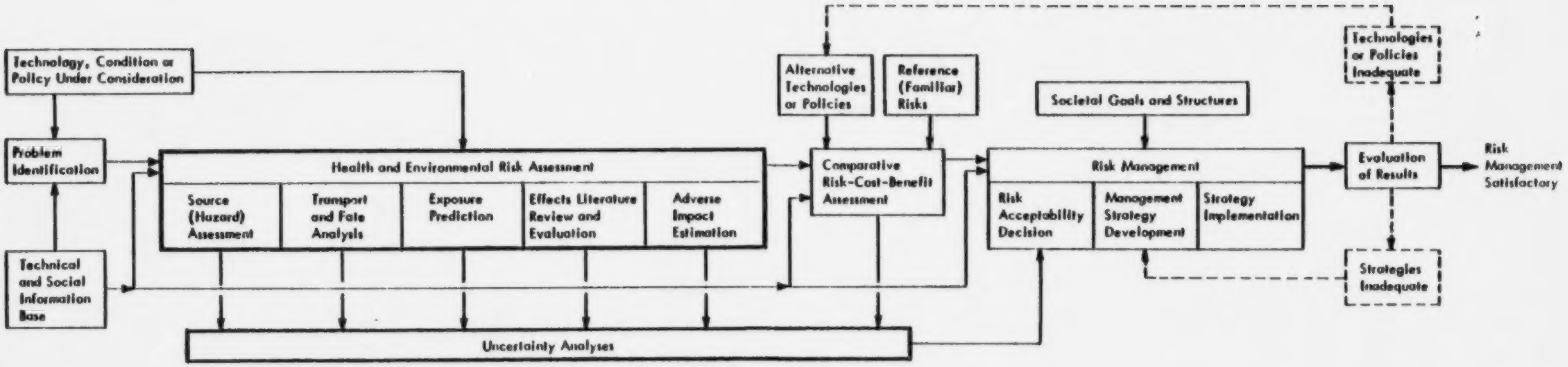
* A reviewer has noted that as soon as one specifies the use of conservative assumptions, a confidence limit on the range of uncertainty, or the use of an upper bound estimate, one is introducing a value judgment into the analysis.

** The "comparative risk assessment" concept described in the proposed "Risk Assessment Research and Demonstration Act" (U.S. Congress, 1985) noted many of these elements. A bill for a "Comprehensive Environmental Risk Management Act" was planned for proposal in the 1987-88 Congress.



Technology, Condition or Policy Under Consideration
Problem Identification
Technical and Social Information Base
Health and Environmental Risk Assessment
Source (Hazard) Assessment
Transport and Fate Analysis
Exposure Prediction
Effects Literature Review and Evaluation
Adverse Impact Estimation
Uncertainty Analyses
Alternative Technologies or Policies
Reference (Familiar) Risks
Comparative Risk-Cost-Benefit Assessment
Societal Goals and Structures
Risk Management
Risk Acceptability Decision
Management Strategy Development
Strategy Implementation
Evaluation of Results
Technologies or Policies Inadequate
Strategies Inadequate
Risk Management Satisfactory

Figure II-1 - Framework for Assessing and Managing Technological Risks

- Comparison of the reduction in risks to health and the environment that may be achieved by one or more technology control options

- Comparison of the risks and costs posed by two or more technologies that serve the same human needs, i.e., provide similar identified benefits*

- Comparison of the risks, costs, and benefits of alternative technologies or technology controls, noting both equity of distribution among stakeholders and net societal effects (reduction of risk is also a benefit)

- Comparison of a given risk with naturally occurring or familiar risks, enabling the decision makers and the public to place the risks, costs, and benefits of alternative technological choices into better perspective

Ideally, a comparative risk-cost-benefit assessment methodology should be characterized by:

- A systematic approach that is sufficiently flexible and nonmechanistic that it can be applied to a variety of decision questions

- A realistic technosocial and institutional view of decision objectives, options, and implementability

- A comprehensive, long range view of risks, costs, and benefits (at minimum, the life cycle of the technology)

- A consistent treatment in the analysis of the technological alternatives and their consequences

- A multidimensional analysis of quite different consequences in summing up the trade-offs among risks, costs, and benefits and in avoiding suboptimization

- A presentation of results that is comprehensible and helpful to the nonexpert, but defensible by scientific standards that simplifies, but does not trivialize; that provides perspective, but does not dictate the decision

In reality, constraints of resources, data, or time may limit the extent of analysis of other technological or policy alternatives.

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* As noted in Section A.2, value judgments enter into the classification of a given consequence as a cost or benefit and also into their perceived importance. Weinbert (1985) has called these "trans-science" issues.

2. Decision making: Risk decision making involves deciding whether or not to actually do something about the source of risk that has been assessed. It requires a combination of substantially science-based estimates* of health and environmental risk, costs, and benefits (developed in preceding steps) with other considerations that affect risk acceptance and aversion, including:

- Nature and reversibility of potential effects
- Special populations at risk (e.g., age, sex, race)
- Voluntariness of risks borne
- Equity of distribution of risks, costs, and benefits
- Potential for low probability events with catastrophic impacts (worst credible case)
- The uncertainties associated with estimates of risk, costs, and benefits
- Public perceptions of risks and of parties-at-interest
- Analysis of socio-political impacts
- Analysis of trade-offs among alternatives
- Related technosocial forecasts
- Availability of regulatory authority and implementation mechanisms
- Relationship with other regulatory needs and priorities, including administrative effectiveness or efficiency

3. Risk management strategies: Approaches to managing risks include a range of individual and social actions taken to avoid, minimize, reduce, limit, or otherwise control the degree of exposure to risk situations or the magnitude of adverse consequences. They can also include actions designed to maximize benefits at a given level of risk. Risk management strategies may include:

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* The estimating procedures, scoping decisions of what effects to include or ignore, etc., may have derived from implicit or explicit value judgments including the use of upper bound estimates vs. best estimates, cut-off criteria for ranges of uncertainty, what to do in selecting worst case scenarios to include or exclude, and what levels of consequences or their probabilities are too low to be of concern to decision makers. Mumpower (1986) has analyzed use of the de minimis strategy in risk management.

- Risk aversion: One selects alternatives that avoid or minimize the risk. Achievement of zero risk is often not possible, but the concept of de minimis or negligible risk is well-recognized by the courts and in daily life.

- Social controls: Governmental agencies, trade associations, and other institutions impose regulations and standards that attempt to limit risks of ongoing activities, products, and conditions.

- Behavioral modifications: An organization attempts to influence behavior to reduce risk, e.g., campaigns to reduce smoking or have health check-ups.

- Engineering controls: The technological system or product is designed to minimize reliance on human attention for safety and thus minimize the chances of human error as a contributing risk factor. Warning systems are also engineering controls. Note, however, that both human errors and concern over potential errors often enter into the design, construction, testing, and maintenance of engineering controls. Man-machine systems involving elements of human control or intervention may sometimes improve a hazardous situation that is unfolding or worsen it through erroneous action. Systems reliability engineering analysis should be used to determine the best mix of human vs. mechanized control of safety systems.

- Administrative controls: An organization limits the nature or degree of exposure to risk for some or all employees, customers, or visitors, e.g., by employment policies that require designated levels of physical or mental abilities; by restricting access to designated hazardous areas

    - Work practices: Employees working at dangerous tasks are required to follow specific procedures and sequences designed to minimize the chances of accident.

    - Personal protection: An individual or group use personal protective devices while being exposed to hazards, e.g., dust mask; an organization decrees certain protective devices for employees or persons in its charge in hazardous situations, e.g., rubber clothing, safety goggles.

    - Education and training: Persons likely to be placed at risk or to be present when others may be at risk are provided special training and education to minimize risk and adverse consequences.

  - * Medical surveillance, treatment, and recordkeeping: An individual or employer monitors the health status of individual(s) that may be exposed to risk situations, and any treatments that are made. Records are kept and reviewed so that indications of trouble can be spotted early.

- Risk spreading and retention: Individuals and corporations have long faced decisions on what levels of risk should be avoided and what levels can be accepted, given that reduction of a risk imposes a cost. When a risk cannot be reduced cost-effectively, a decision may be made to distribute it among several parties so that no one bears an intolerable cost. Such decisions are frequently made in the economic context of establishing an insurance program. Personal health, accident, fire, and liability insurance are common methods of spreading risk, as well as limiting the hours or period of worker exposure.

  Corporations in particular have faced increasingly difficult decisions in the last decade as their liability for occupational and consumer health and safety claims and environmental effects has escalated enormously, and the costs of insurance have reflected the dramatic rise in health care costs and environmental cleanup. "Complete" insurance protection would be prohibitively expensive. Corporate risk managers must therefore balance the insurance program to provide some acceptable level of risk protection without unacceptably draining cash resources. Depending on the ability and willingness to bear risks, a risk manager may take two major factors into account: (a) the aggregate maximum amount of loss that the company is willing to bear from all of its risk sources; and (b) the specific levels of risk for each risk source that the company is willing to retain in view of remedial action or insurance costs.

4. Decision implementation: Successful implementation of the decision and strategy is the final component of the risk management process. It may include one or all of the following:

- Determining organizational procedures to be employed and timetables to be followed
- Promulgating policies, guidelines, criteria, standards, rules, and other regulatory change
- Establishing reporting requirements and schedules
- Determining inspection and monitoring needs

- Establishing effective forums for receiving public comment and other mechanisms for negotiation and dispute resolution
- Establishing enforcement and penalty procedures
- Implementing periodic review of decisions and strategies in light of new information and progress to date

The risk assessment/management process has been described here in a sequential order, but in reality, it is usually an iterative process with multiple feedback loops.* Uncertainty analysis should be a part of each step in the assessment: uncertainties should be identified and quantified throughout and aggregated across the process.

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* A more proscriptive decision tree approach to hazardous waste site mitigation was reported by the State of California after the present approach was formulated (CDHS, 1986).

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III. APPROACH TO COMPARATIVE RISK ASSESSMENT OF HAZARDOUS WASTE MANAGEMENT ALTERNATIVES

An approach for assessing and comparing the risks to human health and the environment of hazardous waste management alternatives is outlined in this chapter. Methodological objectives are briefly noted, followed by a summary of the methodological framework developed in this study.

A. Methodological Objectives

The methodology should be based on the objectives and scope of the study stated in Chapter I and should fit within the framework for assessing and managing risks outlined in Chapter II. A rationale and guidelines for developing a methodology and several considerations in bounding an assessment are discussed briefly below.

1. Rationale and guidelines: Hazardous waste management decisions will typically involve a choice among alternatives, rather than a "yes" or "no" choice. Therefore, the goal of the methodology is to provide information so that the decision maker can compare the likely (and possible) outcomes of alternative decisions. An objective is to incorporate techniques that will yield scientifically defensible comparative risk assessments, and to avoid mixing in components more properly reserved to the risk management portion of the overall regulatory process. Key points in the rationale are:

- The methodology should be comprehensive and consistent, yet flexible.
- The methodology should minimize introduction of personal values and identify unavoidable value-laden decisions and assumptions.
- The methodology should yield information on the most likely outcomes for each option, and also on the uncertainties in such estimates for all options considered. All are needed in risk-based decision making.‡ (Note that the choice of options will reflect someone's values.)
- Comprehensiveness requires that the assessment of each option consider all kinds of releases, transport routes, and health and environmental effects (not just carcinogenicity, for example) for the life cycle of the technology or beyond if there are long term effects. The assessment of effects, particularly secondary or higher order effects, will be limited by time, resources and data. (Note that the allocation of time and resources can reflect values.)

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‡ The cost-benefit analyses in support of decision making should be similarly comprehensive, consistent and explicit about uncertainties.

- Consistency requires that in analyzing the risks, comparable contributing factors be treated comparably for each option. For example, assumptions must be consistent regarding quantities and compositions of wastes, scale of disposal technologies, remedial or corrective actions taken, temporal aspects, and dose response relationships. Uncertainties must also be consistently treated.

- The methodology must be flexible because of the variability of the hazardous waste problems and of the data available for assessments. For example, different assessments may address different: wastes; treatment and disposal technologies; modes of toxicant release and transport; exposure conditions; and health or environmental effects.

- Flexibility requires that the methodology should be essentially modular across the several stages of the assessment process in order to respond to differences in availability and applicability of data or analytical techniques. One should be able to incorporate refinements or extensions of a presently proposed technique, alternative techniques, or new techniques as they become available.

- The methodology should yield quantitative results when necessary data are available and yield the most useful results possible when data (or the time and resources needed to compile data) are limited.

- Estimation of the most likely outcome requires that the methodology be oriented throughout to the development of "best" estimates [often maximum likelihood estimates (MLEs)] for each factor rather than "worst case" or "worst credible case" estimates. The best estimates for the contributing factors should then be combined to provide a best estimate for each kind of effect. The analysis should not inconsistently mix best estimates (or MLEs) for some factors with upper confidence limit estimates (e.g., 99%) for other factors.‡ The resulting estimate of overall effect would be at some ill-defined point between an MLE and a worst case estimate. The analysis should, however, address confidence limits in the uncertainty analysis, and both the best estimate and the uncertainty range should be provided to the decision maker.

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‡ The uncertainty for each factor can be stated to within one standard deviation ($\pm 1\ \sigma$) of the best estimate or some higher confidence interval such as $2\ \sigma$ or $3\ \sigma$. The larger intervals after aggregation will tend to increase the overlap of risk estimates for the options being compared, and the choice of interval probably won't make a big difference in most decisions between technologies.

- * Analysis of uncertainties must consider both systematic and random sources of error. Uncertainties should be estimated for each factor contributing to the risk for each option assessed, and should be stated with the same confidence bounds for all factors. The uncertainties should be aggregated across the entire assessment for each option. Aggregated uncertainties should be compared both as total uncertainty and as relative uncertainty for the options. If a particular cause of uncertainty is common across the options, it can be cancelled in making relative risk comparisons, since it will not affect the ranking of alternatives. However, total uncertainty must be considered if a cut-off risk level is to be determined.

- * The results should be summarized in a concise form with sufficient clarity to be useful to decision makers who are not technical experts, but should be supported by enough technical detail to permit analysis of the procedures used and assumptions required.

- * Failure to be comprehensive and consistent throughout the assessment can lead to decisions that are less protective of health and the environment, and possibly also more costly to society than another decision would have been. Assessments involving mixed chemical wastes or disposal options that could lead to exposures to different chemicals with different health effects must be particularly careful to avoid inconsistent analyses that could lead to perverse decisions.

2. Bounding the assessment: The general bounds of the assessment will be indicated by the nature of the decision problem, but the assessment team may be required to establish other bounds so that the most useful results can be obtained with the time and resource available. Bounding decisions could involve:

- Wastes to be considered - Is one or more specific waste sources already identified, or does the project team need to identify wastes representative of some part of the overall waste disposal problem? Is the waste defined already or does the project team need to define representative quantity and composition? The larger the amount and the greater the diversity of wastes, the more effort required.

- Waste management alternatives - Are one or more waste management alternatives already defined, or does the project team need to identify reasonable alternatives for assessment? Are corrective or remedial actions in event of release to the environment to be defined? The greater the number and diversity of alternatives, the greater the effort.

- Sites to be considered - Have waste generation and disposal sites been defined already, or does the project team need to develop representative sites? The greater the number and diversity of sites, the greater the effort required.

- Temporal considerations - Have the time periods of waste disposal, exposure assessment and health impacts been defined, or does the project team need to assume reasonable periods? The greater the time periods in general, the greater the uncertainties.

A simpler methodology, while a highly desirable goal, appears necessarily to require more restrictive bounding and a larger number of assumptions to be built in.

B. Methodological Framework

The methodology outlined below is described in greater detail in Chapter IV and is based on the literature reviews and discussions in Chapters V through X. It is intended to be as generic as practicable, but to permit modifications in accord with the nature of particular assessment problems and with the quality of the data available. Important features are:

- It provides a modular framework for a series of steps, most of which must be performed in given assessments.
- It can assess the consequences of disposing of specific wastes at specific sites with specific technologies, through use of actual case data or carefully constructed scenarios.
- It contains procedures for selecting among available analytical techniques for each step so that maximum use can be made of the data available.
- It analyzes uncertainties in all steps and aggregates them across all steps in each assessment.

The general framework for the health and environmental risk assessment consists broadly of the seven steps as follows:

- Source Assessment (Hazard Characterization)
- Environmental Transport and Fate Analysis
- Exposure Prediction
- Health and Environmental Effects Analysis
- Adverse Impact Estimation and Summation
- Uncertainty Analysis
- Report and Compare the Results as Appropriate

Each of these steps contains more than one element, however, so that the overall scope of the risk assessment can contain many elements, depending on the decision problem. Typical activities under each step are as follows:

- Source assessment (hazard characterization) requires characterization of the source of environmental contaminants, including:
    - Identification of chemicals present
    - Preliminary identification of their physical, chemical, and biological properties of concern
    - Analysis of the technologies and practices that may result in release of contaminants to the environment and identification of release points and routes
    - Quantification of source strength, i.e., the rate, concentration, quantity, and form of hazardous constituent released
- Environmental transport and fate analysis involves estimation of the manner in which the contaminants move and react in the environment, including:
    - Identification of major environmental transport routes and transformation pathways for chemicals of concern
    - Estimation of concentrations of chemicals (or their hazardous transformation products) along these routes over time
    - Identification of locations along these routes where the chemicals may reach susceptible populations
- Exposure prediction involves estimation of the degree to which pollutants reach humans or other organisms, including:
    - Estimation of numbers of people or organisms that may be contacted, including sensitive subpopulations
    - Prediction of frequency, intensity, and duration of the exposures that may occur for populations or subpopulations
- Health and environmental effects analysis involves:
    - Intensive review of the literature on the health and environmental effects for the chemicals of concern
    - Identification of ranges of responses known, and especially those that could occur at predicted environmental exposures
    - Development of chemical-specific dose-response relationships for those effects of concern that are to be assessed

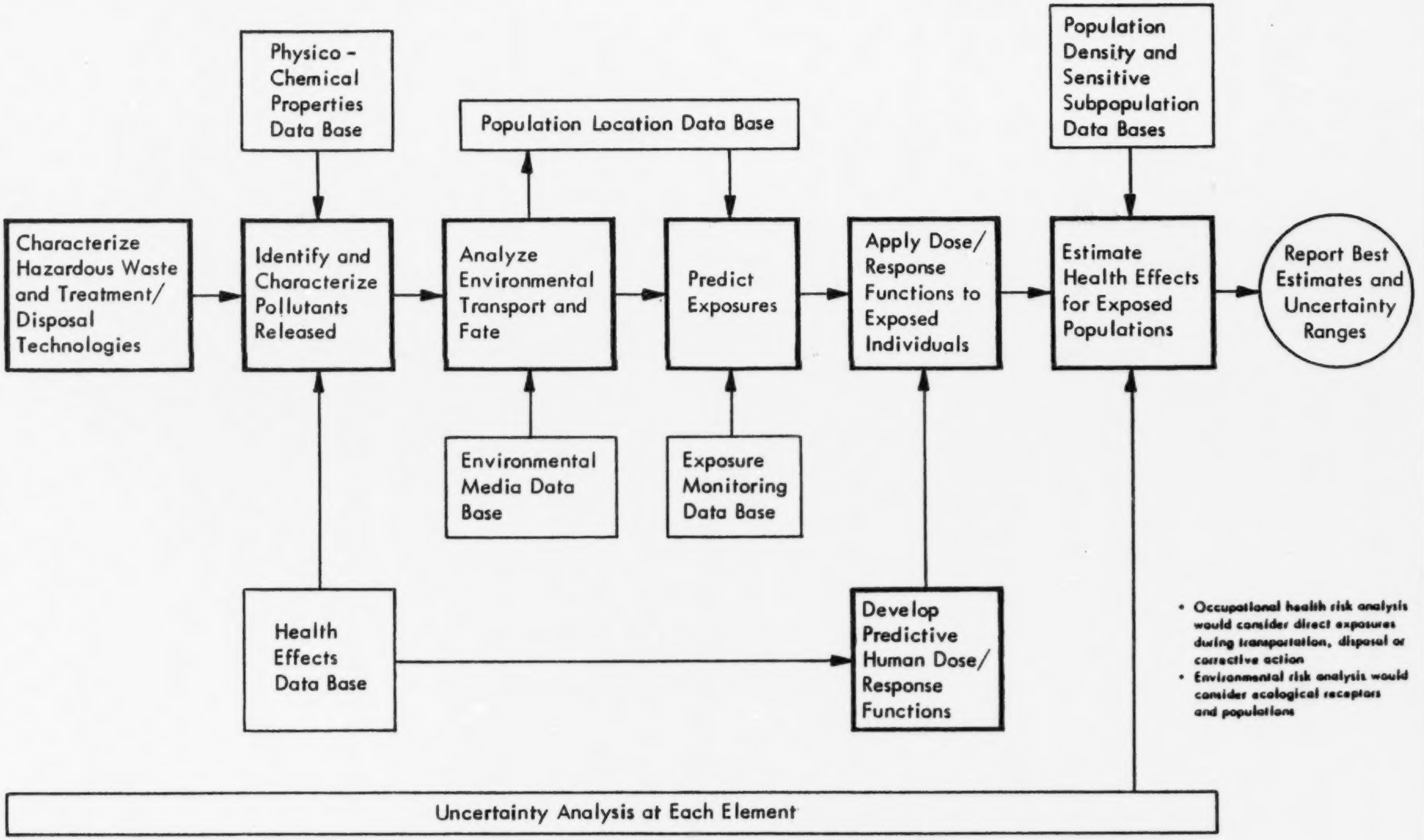
  - Development (through selected extrapolation methods) of risk factors for specific predicted environmental doses

- Adverse impact estimation and summation is an integrative step that involves estimation of the probabilities and extents of adverse health and environmental effects actually expected from the predicted exposures, including:
  - Application of dose-response functions to exposed individuals by exposure group
  - Identification of any sensitive subpopulations of concern
  - Best estimates of the risks for each effect in each subpopulation
  - Best estimates of the total number of cases of each effect

- Uncertainty analysis involves:
  - Identification and evaluation of uncertainties of all factors that enter into the risk assessment
  - Sensitivity analysis of key factors
  - Quantify uncertainty of factors at same confidence levels
  - Aggregate uncertainties of all factors across steps in risk assessment

- Report and communicate results involves:
  - Compile best risk estimates and uncertainty ranges for each waste management alternative assessed
  - Compare best estimates and uncertainties across alternatives
  - Compare, as appropriate, costs or other aspects of alternatives
  - Describe the assessment and results in several formats, including detailed technical report, extended and concise summaries, or oral presentations, as appropriate, to serve different audiences

The interrelationships of typical elements likely to be required in assessing public health risks of hazardous waste disposal options are shown schematically in Figure III-1. (Additional elements would be desirable in assessments of occupational health and ecological risks.) In order to make meaningful health effects estimations (the last box on the right in Figure III-1) for each waste management alternative, the assessment must be


Physico - Chemical Properties Data Base
Population Location Data Base
Population Density and Sensitive Subpopulation Data Bases
Characterize Hazardous Waste and Treatment/ Disposal Technologies
Identify and Characterize Pollutants Released
Analyze Environmental Transport and Fate
Predict Exposures
Apply Dose/ Response Functions to Exposed Individuals
Estimate Health Effects for Exposed Populations
Report Best Estimates and Uncertainty Ranges
Environmental Media Data Base
Exposure Monitoring Data Base
Health Effects Data Base
Develop Predictive Human Dose/ Response Functions
Uncertainty Analysis at Each Element

- Occupational health risk analysis would consider direct exposures during transportation, disposal or corrective action
- Environmental risk analysis would consider ecological receptors and populations

Source: MRI.

Figure III-1 - Elements in Health Risk Assessment of Hazardous Waste Disposal Methods

carefully bounded, appropriate data must be compiled, analytical techniques must be selected and calculations made, and conclusions drawn in a scientifically defensible manner. Chapter IV develops these steps and elements further.

IV. AN INTEGRATED COMPARATIVE RISK ASSESSMENT METHODOLOGY

A methodology for assessing and comparing the risks to human health and the environment of hazardous waste management alternatives is developed in this chapter. It is based on the methodological concepts and framework outlined in Chapter III and on the results of the reviews and analyses of component steps given in Chapters V through X. Extensive references are provided in those chapters. The methodology should be applied consistently to each of the alternatives so that their risks can be compared realistically.

MRI's suggested framework for health and environmental risks assessments of hazardous waste management alternatives consists of seven major steps: (1) assess pollutant sources and releases; (2) estimate transport and fate of pollutants in the environment; (3) assess exposures of humans, other species, or other things to the pollutants; (4) review and evaluate the literature base for the pollutants and select or develop predictive models for adverse impacts; (5) estimate actual impacts on individuals and populations of projected exposures to these substances; (6) analyze uncertainties for each step and aggregate the uncertainty across all steps; and (7) summarize and report the results.

A. Source Assessment (Hazardous Characterization)

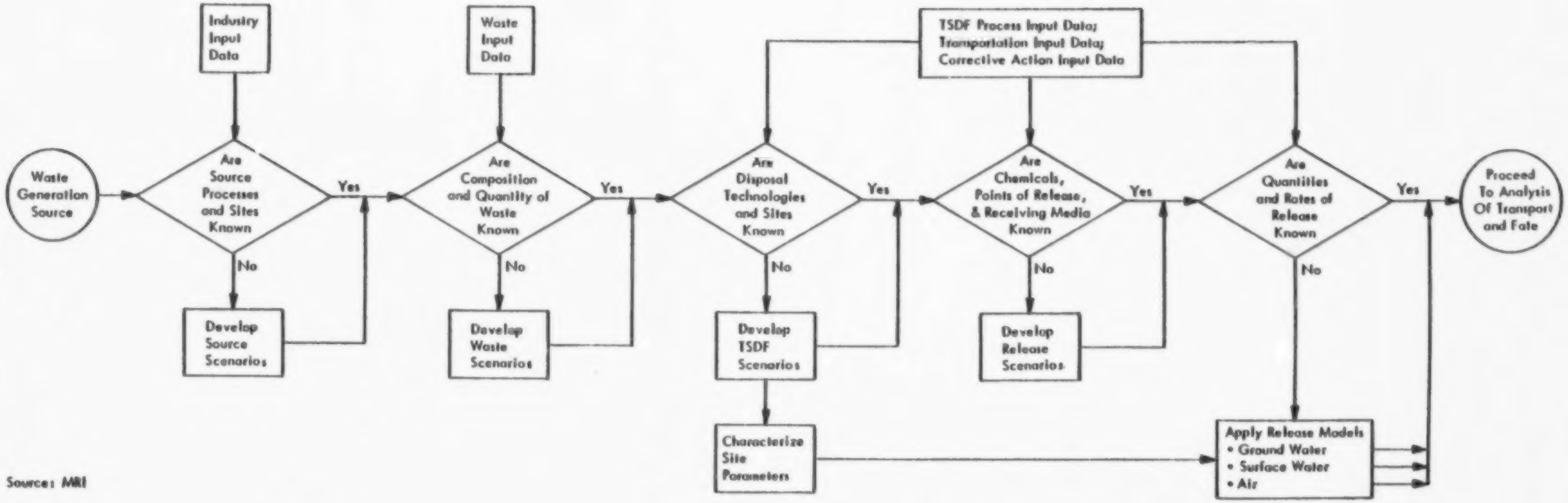
The pollutants entering the environment from the source must first be determined. In some assessments, the nature of the pollutants, their quantities, points of release, and the receiving environmental media may all be stipulated in the scope of work for the study. Here the "nature of the pollutant" should specify at a minimum the chemicals present; their general physical and biological properties must be found in the literature if not provided. In other assessments, the source of the waste (e.g., an industrial process) and disposal practices in use may be stipulated, but the analyst will have to estimate pollutant releases. In still another case, the assessment team may have to define a general scenario for analysis, including waste source, composition and quantity, disposal technology, and pollutant releases. Guidelines for developing such scenarios are given in Chapter V and illustrated with examples in Appendix B. Described below is our general approach to source assessment followed by a discussion of special problems arising from corrective actions and catastrophes.

1. General approach: Important considerations in the source assessment step are summarized in Table IV-1. A schema for performing an assessment of hazardous wastes as sources of environmental pollution is shown in Figure IV-1. (The schema assumes that time periods for waste generation, disposal and pollutant release have been defined; if not they must first be denoted.) Key activities in the source assessment include:

TABLE IV-1

IMPORTANT CONSIDERATIONS IN HAZARDOUS WASTE DISPOSAL SOURCE ASSESSMENT

Characterize Wastes		Characterize Releases			
Generation Activities	Wastes of Concern	Release Mechanisms	Receiving Media	Hazard Designation	Release Quantification
Production and distribution processes	Locations	Emissions Vapors Particulates	Air Local Regional Global	Chemicals	Chemicals
Product use patterns	Quantities	Effluents Solutions Suspensions	Surface waters Watersheds Impoundments Estuaries Seas and oceans	Quantities available	Rates
Hazardous waste TSDFs	Compositions	Land disposal	Groundwater zones Unsaturated Saturated	Properties Physical Chemical Biological	Quantities
	Properties	Accidents Leaks Spills Explosions Fires Floods Winds	Land Surface Subsurface Deep strata	Temporal considerations	Physico-chemical form


Waste Generation Source
Industry Input Data
Are Source Processes and Sites Known
Yes
No
Develop Source Scenarios
Waste Input Data
Are Composition and Quantity of Waste Known
Yes
No
Develop Waste Scenarios
TSDF Process Input Data; Transportation Input Data; Corrective Action Input Data
Are Disposal Technologies and Sites Known
Yes
No
Develop TSDF Scenarios
Characterize Site Parameters
Are Chemicals, Points of Release, & Receiving Media Known
Yes
No
Develop Release Scenarios
Are Quantities and Rates of Release Known
Yes
No
Apply Release Models
• Ground Water
• Surface Water
• Air
Proceed To Analysis Of Transport and Fate

Source: MRI

Figure IV-1 - Schema for Assessing Hazardous Wastes as Sources of Environmental Pollution

- Characterize hazardous substance source of concern. Include as necessary waste generation activities (e.g., production and distribution processes; product use patterns) and hazardous waste treatment storage and disposal facilities (TSDFs).
- Characterize location, generation rate, quantity, composition, and properties of waste to be assessed. Composition includes qualitative and quantitative information on the specific chemicals present.
- Characterize release of contaminants to the environment from the source. Identify release mechanisms, quantities, and the receiving media.
- Identify the chemicals likely to be released based on preliminary knowledge of their physical and chemical properties and their concentrations in the waste.
- Make a preliminary review of the toxicological and ecological properties of those chemicals likely to be released in significant amounts.
- Designate for detailed assessment those chemicals which are present in such quantities and have such properties that their release may cause significant adverse impacts. Preliminary considerations of receiving media and receptor populations will probably be required here. These designations should be reevaluated during the impact analysis.
- Quantify the source; i.e., estimate the rate, concentration, quantity, and physical chemical form of each hazardous constituent released to each receiving medium.

In practice, the source assessment should use the best available information and data in constructing scenarios and making calculations. Search and retrieval of information for source and waste characterization may require extensive literature search and personal contacts. Sources of data, methods of estimation, and reasons for assumptions should be carefully documented. Information should also be referenced pertaining to the uncertainty range about best estimates for each value.

Release quantification may well be the most difficult part of source assessment unless simplifying assumptions are made. Release may be site as well as facility specific. Particularly difficult may be releases during transport or at storage and transfer points.

Considerable data are now available for discharges and emissions from many typical industrial processes and TSDFs, but the data may not be definitive in a given case, and very little data may be available in others. For example, emissions to air have been measured for many incineration facilities, but much uncertainty exists over the level of chlorodioxin release under many operating conditions. Similarly, fugitive particulate emissions to air from roadways used by vehicles have been measured, but few data are available on the amount of adsorbed dioxin that might be released by this mode in a clean-up operation. Discharges to surface waters by rainwater runoff can probably be confidently estimated for some typical older facilities, but perhaps not for others. Estimation of releases to groundwater and air from landfills of various design is particularly limited by the immaturity of the development of data bases and predictive methods. At present, the landfill release model being developed by the EPA Office of Solid Waste and Pope-Reid Associates appears to be the best available for estimating losses to groundwater (see Chapter V).

2. Special scenarios: The possibilities that corrective actions will be taken when releases to the environment are discovered poses difficult methodological problems in assessing risks, costs, and the benefit impacts of TSDFs. Problems of a different nature are posed by the possibility of operation under upset conditions or of catastrophic failures. All of these problems require scenario approaches as discussed below.

a. Corrective action scenarios: Under RCRA regulations 40 CFR Part 264.100, corrective action is required when monitoring wells are found to contain hazardous constituents that exceed their respective concentration limits. Corrective actions can range from groundwater pumping to retrieval and redisposal of the waste. Including future corrective actions in the risk assessment and cost analysis poses methodological difficulties in making a comparative assessment of alternative disposal technologies and approaches. These difficulties arise from two areas: temporal factors and the efficiency of the given corrective action.

(1) Temporal factors: There are two kinds of time-related problems. The first involves assumptions about future societal requirements and available technologies. These include the sensitivity of leak detection methods, the levels and kinds of corrective action that may be required, and the technologies that may be available for implementation and their costs. One technique for addressing this problem is to assume that presently available analytical techniques, regulations, technologies, and costs could be applied. Alternatively, different conditions could be defined.

The second kind of time-related problem involves assumptions about the timing of corrective action and is more difficult to address. Corrective action is required if leakage from a landfill is detected while the facility is receiving hazardous wastes or during a 30-year post-closure period of monitoring and care by the operator. The operator must then maintain corrective action for as long as a groundwater problem exists, even indefinitely past the normal post-closure care period. In a 200-year scenario for analysis, for example, a landfill operated for 20 years and found to be leaking 29 years into the post-closure period could require corrective action for up to 151 years. On the other hand, if no leakage had been detected by the end of the 30-year post-closure period, the operator's responsibility to monitor the site would cease under current regulations. Responsibility for providing corrective action might possibly also cease, but the outcome would be uncertain.

The methodological problem in comparative risk assessment is that the risks to health and the cost to the operator may vary greatly depending on whether or not a leak is detected and on the type of corrective action taken. Furthermore, leaks (or accidents) have a probability distribution over time, and the few leaks occurring early may have many different (probably greater) impacts than those occurring later. The detection of a liner leak during the waste deposition period, for example, may dictate that the landfill be excavated* and repairs made to the liner and its base.** The possible health effects and cost of such remedial actions could vary widely with the scenario chosen and could conceivably be substantial. In general, however, changes in health impacts for corrective actions for leaking landfills or impoundments during a 20-year operating period can be reasonably assumed to be negligible. The probability of leaking during the operating period is small, and is accounted for in the Pope-Reid model used to estimate release of pollutants from the landfill. The model assumes a degree of preclosure repairs of detected leaks which reduces somewhat the volume of leachate from the landfill that would otherwise occur from early liner failures. If costs are being analyzed, the assessments should state explicitly if preclosure repair costs are included or omitted.

The detection of a liner leak during the post-closure monitoring period also requires some type of corrective action. An assumption can be reasonably be made that only the minimum corrective action will be taken to satisfy the hazardous waste disposal regulations (40 CFR 264). In some cases, groundwater pumping can be assumed to be the only corrective action taken. In others, excavation and repair may need to be assumed. In still others, consequence mitigation measures, such as treatment of water supplies drawn from contaminated aquifers, may need to be considered.*** In all cases, the health effects and cost analyses should state explicitly what has been included and what has been omitted.

Liner leaks that have not been detected by the end of the post-closure care period or that develop during the post-closure care period pose a further methodological problem. In some studies, one might want to assume that no corrective action was taken because there was little probability of discovering a leak after 50 years (monitoring by the operator ceases 30 years after closure). In reality, of course, the discovery of a major leak in the post-closure care years that posed serious human health hazards to the public would almost certainly receive some kind of corrective action, probably under the Superfund legislation, i.e., CERCLA of 1980 and SARA of 1986.‡ Again, all assumptions should be explicitly stated.

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* The appearance of contaminated leachate in the leachate collection system may be sufficient reason to dictate action beyond simple pumping.

** In practice, the facility may be closed by the operator or government and the wastes relocated.

***In reality additional treatment would probably be performed if deemed advisable.

‡ If one did not assume such subsequent corrective action, a paradox would exist: a poorly designed landfill that failed quickly but was detected and repaired would be safer than a better designed one that failed later.

(2) Efficiency of corrective action: The efficiency of corrective action also poses a substantial methodological problem. The objective of the methodology is to compare the risks and costs of alternative hazardous waste disposal technologies. Corrective actions may vary widely, however, in type and degree of application, and may have corresponding variations in cost and efficiency; in general, the greater the health protection required, the greater the cost. Safety-cost trade-offs need to be explored in reaching the most cost-effective decisions to serve societal values, especially in Superfund site cleanups where the resources are limited. In theory, complete protection can be provided at some cost, even if it means using public funds to relocate a threatened population.*

The assumption of such extreme measures of corrective action to provide complete protection may not be helpful in many risk assessments, however. If health risks are nominally reduced to zero for all scenarios, useful comparisons of health risks could not be made. Only the cost estimates could be compared, and these would have been highly sensitive to the assumptions regarding corrective action. Hence a more useful approach may be to assume a degree of corrective action that is reasonably attainable with present technology, but which does not necessarily provide 100% protection.

b. Catastrophe scenarios: Catastrophic releases of hazardous substances during storage, processing, or transport of large quantities of wastes pose serious occasions of intense occupational and public exposure to health and safety risks and of substantial local ecological damage. Such releases could be initiated by either natural events, such as floods, tornadoes, lightning, and earthquakes, or human activities such as spills, fires, transportation accidents on land or sea, and acts of vandalism or terrorism. The present methodology focuses on assessing risks of typical releases from TSDFs. The magnitude and probability of catastrophic releases, however, pose special problems that should not be ignored in a comprehensive assessment. In particular, results can depend on what assumptions are made concerning contingency accident management plans and consequence mitigation measures that are at hand.

Issues, methods, and case studies involving low probability but high consequence risks were described in over 40 papers at a recent meeting (see Chapter V). The methodology for assessing such risks is less developed than that for more typical risks, and further development of it is beyond the scope of the present study. In general, scenario approaches are required, but the outcome is quite dependent on assumptions about technologies, sites, timing, operation of failure prevention/detection measures, and human behavior. One cannot assess scenarios for every combination of events, but one can develop reasonable scenarios. Persons actually responsible for emergency response actions frequently develop and train for such scenarios.

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* Over $33 million was expended by EPA and the Federal Emergency Management Agency to relocate a population of 2,000 at dioxin-contaminated Times Beach, Missouri.

In the case of hazardous waste disposal, releases, exposures, and impacts will be dependent on the nature of the waste in a given assessment, on the site of catastrophic release, and on assumptions concerning the timing and efficiency of protective and corrective actions. In some cases, the nature of the waste and the disposal technologies might make negligible the probability of catastrophic releases from many or even most causes. For example, a nonflammable sludge of low volatility, low solubility in water, and high viscosity could be cleaned up with minimum risk in event of a large spill from an overturned truck. In view of the usual time and resource limitations, efforts to assess such risks could be reasonably minimized in the health and cost assessment.

On the other hand, attention may be required for the risks of flooding during cleanup of an old hazardous waste disposal site or for the risks of loading/unloading activities in transporting wastes for at-sea incineration. At a minimum, transportation risks should be discussed qualitatively; subsequent quantitative analysis may be desirable before ultimate decisions are reached. The qualitative analysis should note the worst reasonable case scenario, e.g., a maximum release at the most populous or most difficult to clean-up point in the route. In general, the more decentralized the hazardous wastes, the lower the risks of catastrophic release, the more centralized the waste disposal technology, the greater the potential for catastrophe.

B. Environmental Transport and Fate Analysis

The movement and interactions of pollutants entering the environment are affected by physicochemical and biological processes which can vary with the natures of the pollutants, how they are released, and the media they enter. These conditions will already have been defined in the source assessment. The environmental processes will also depend on characteristics of specific sites, starting with the area immediately around the source and extending to areas where populations may be exposed. Hence the next element in assessing the risks of hazardous waste management alternatives is characterization of the sites under study. Depending on the waste and site characterizations, appropriate transport models are then selected to estimate the movement of pollutants to populations. Site characterizations and model selection are discussed below.

1. Site characterization: The general data requirements for modeling transport and fate of chemicals released into the environment and sources for finding such information are discussed in Section VI.A. Requirements could include physical characterstics of the TSDF and surrounding terrain, physicochemical properties of soils, water and air, and biological characteristics of the area. The checklists in Table IV-2 of processes affecting transport and fate of environmental contaminants suggest the range of possible requirements.

TABLE IV-2

PROCESSES AFFECTING ENVIRONMENTAL TRANSPORT AND FATE OF POLLUTANTS

Physicochemical Processes

- Transfer
- Dispersion
- Dilution
- Adsorption
  - Activation
  - Stabilization
  - Immobilization
- Reaction
  - Hydrolysis
  - Oxidation
  - Reduction
  - Photolysis
  - Degradation
  - Decomposition
  - Radioactive decay
- Intermedia transfers
  - Volatilization
  - Dusting
  - Erosion
  - Sedimentation
  - Precipitation
  - Solution
  - Accumulation

Biological Processes

- Uptake
  - Terrestrial plants
  - Aquatic species
  - Microorganisms
  - Other biota
- Metabolism
  - Activation
  - Conversion
  - Degradation
  - Decomposition
  - Excretion
  - Toxic Effects
- Bioaccumulation
- Biomagnification in food chains
- Interbiotic/intermedia transfers

For some decision-making purposes, several scenarios of representative characteristics might be a useful basis of analysis, but in other cases actual or carefully estimated data on characteristics will be essential. Complete site characterization requires significant time and resources. The effort can be minimized by considering only those characteristics dictated by the nature of the pollutant and the receiving media. Thus if release from the TSDF is entirely to groundwaters, wind speed and direction at the site will not be required. Conversely, if the pollutant chemical is known to be tightly adsorbed in soils, subsurface hydrogeological information might not be needed, but air data would. Note that bioavailability of a chemical can change with the soil conditions. If the pollutant is permanently persistent, consideration of metabolizing organisms may be unnecessary (although biotransformations may require analysis).

Temporal assumptions should be explicitly stated. That is, the analyst should say if the characteristics of the site are assumed to stay the same or to change over the time horizon of the assessment.

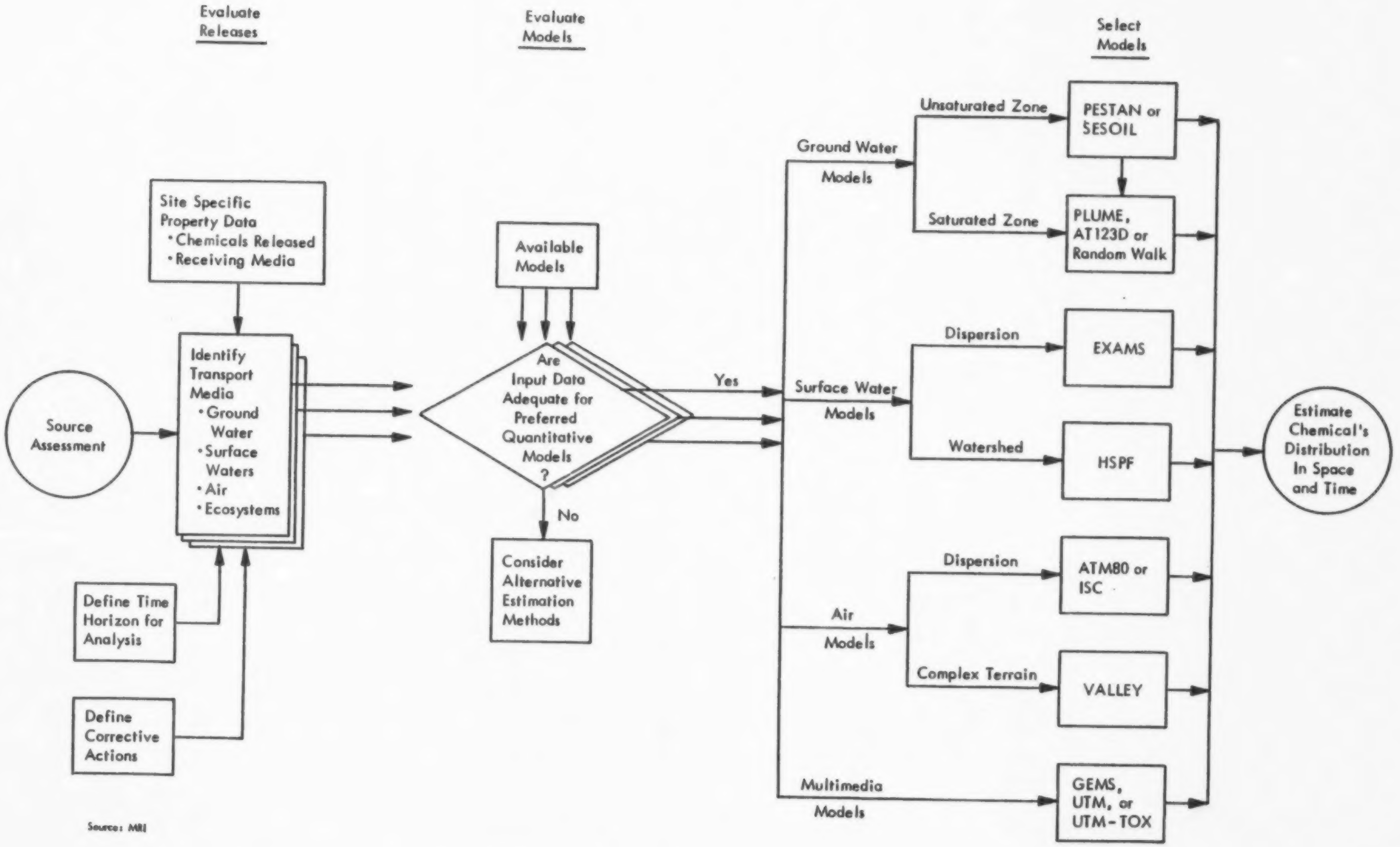
2. Model selection: The selection of models for predicting environmental transport and fate will depend not only on the nature of the pollutant and the receiving media, as noted above, but also on the quality and quantity of the data base available. To be as generically useful as possible a selected model should be able to utilize data likely to be available in most assessment problems and yield quantitative calculations of the concentrations of a contaminant as it moves through a particular medium of interest. In addition a selected model should be well-validated, if possible, in the context of a number of representative case studies.

Available models for the main environmental compartments are discussed and compared in Chapter VI. Many of these models were developed for special problems in a single medium while others have a broad, multimedia scope. Their capabilities and limitations vary substantially. The choice of models in a given analysis depends not only on the scope of the problems and the level of detail and certainty desired in the results, but also on the data, time, and resources available for the job. A schema for helping select appropriate models for environmental transport analysis in exposure assessment of hazardous waste TSDFs is given in Figure IV-2. Preferred models for groundwater, surface waters, and air dispersion are summarized below.

(a) Groundwater models: Prediction of transport of pollutants in subsurface waters should address sequentially movements in the upper, unsaturated or partially saturated vadose zone and in the deeper, saturated zones or aquifers. Both zones can be addressed by either analytical or numerical mathematical models (see Chapter VI); the choice in a given case depending on the data available and outputs desired. Ranking models can also be of use in special cases as discussed below.

(1) Preferred unsaturated zone models: The recommended models for estimating contaminant residence time and movement in the unsaturated zone are analytical mathematical models such as PESTAN or SESOIL (see Section VI.B.1.c). A mathematical hydraulic expression such as that developed by McWhorter and Nelson can be useful in situations in which the soil is sandy-gravelly, and groundwater levels within a few meters of the surface. Mathematical transport models may be inapplicable to some combinations of pollutants and unsaturated zone soils, e.g., large releases of some highly chlorinated solvents into clay strata can cause fracturing and rapid transport by channeling. In cases where models or equations cannot be used, estimates of rate of transport and residence time have to be made. For example, if extensive channeling is predicted, transit time in the unsaturated zone might be assumed to be negligible.

(2) Preferred saturated zone models: The complexity required in the exposure and risk assessment scenarios influences the selection of the groundwater transport model. In general, an analytical model will be able to model a contaminant plume in a homogeneous aquifer, but will not be


Evaluate Releases
Evaluate Models
Select Models
Source Assessment
Site Specific Property Data
•Chemicals Released
•Receiving Media
Identify Transport Media
•Ground Water
•Surface Waters
•Air
•Ecosystems
Define Time Horizon for Analysis
Define Corrective Actions
Available Models
Are Input Data Adequate for Preferred Quantitative Models ?
Yes
No
Consider Alternative Estimation Methods
Ground Water Models
Unsaturated Zone
Saturated Zone
Surface Water Models
Dispersion
Watershed
Air Models
Dispersion
Complex Terrain
Multimedia Models
PESTAN or SESOIL
PLUME, AT123D or Random Walk
EXAMS
HSPF
ATM80 or ISC
VALLEY
GEMS, UTM, or UTM-TOX
Estimate Chemical's Distribution In Space and Time

Source: MRI

Figure IV-2 - Schema for Selection of Models for Analysis of Transport and Fate of Pollutants Entering the Environment

able to show the effects of adding corrective action recovery wells to the scenario. A numerical model will be able to predict the effect of corrective action wells on the contaminant plume but requires significant increases in input data, allocation of time and funds, and, possibly, computer resources. Many numerical models are able to handle heterogeneous aquifers under water table, artesian, or leaky artesian conditions.

The decision of whether to use an analytical model or a numerical model can depend on the quantity of available data and on the availability of personnel knowledgeable in the use of a particular numerical model. It may also depend on the need to use the least time-consuming technique to provide good initial estimates of the dispersion, advection, and adsorption characteristics of a specific disposal site. An analytical model is highly desirable and useful for screening alternative waste disposal sites, for example, and for detailed planning and design of field measurements and monitoring programs. However, it may not be as useful as a numerical model in predicting specific conditions at points of exposure.

Models that can be recommended for use in a generic methodology are:

- A combination of two analytical models, PESTAN for unsaturated flow and PLUME for saturated flow, can be superior for some exposure assessments because of their user friendliness and minimal data requirements. The FEMWATER/FEMWASTE couple appears to be another useful system.

- The analytical model AT123D rates well because it can provide one-, two-, or three-dimensional modeling of a contaminant plume; data needs are greater with the AT123D, but not unmanageable.

- The numerical Random Walk Solute Transport Model or TRANS may be preferred for certain exposure assessments because it permits a determination of the effects on the contaminant plume of corrective action wells, or a large-capacity water-supply well-field near the source site. The Random Walk Model requires a greater amount of groundwater data (e.g., well capacities, well spacings), but most aquifer parameters are similar to those required by AT123D. Note that in some cases characterization of present or likely future groundwater withdrawals from the aquifer, recharge rates, and water table levels or depletions may be important to the impact assessment.

(3) Ranking-type models: Although not strictly groundwater transport models, ranking-type models can often provide the best available measure of potential groundwater problems in emergency situations. Combination of contamination ranking models and the groundwater-related portions of hazardous waste site ranking models can provide a method for analyzing an immediate problem. Potentially useful ranking models include: the current forms of the LeGrand Model; the MITRE system; and the JRB model (see Section VI.B.2). These models require minimal data input, equipment, time, and expense, and yield quasi-quantitative site evaluations.

Data needs for ranking-type models are less rigorous than the corresponding inputs required for mathematical models. The modest data requirements of ranking models make them easier to use in the field than analytical or numerical mathematical models. Limitations in using ranking models in risk assessments include the lack of definitive quantitative output (e.g., potential contaminant concentrations at points of human contact), and inability to allow for complex physical, chemical, and biological factors.

b. Surface water models: Prediction of transport of pollutants in surface waters should separately address dispersion of spills in streams (point sources) and watershed runoff (nonpoint sources).

(1) Preferred dispersion models: The recommended model for computing fate, persistence, and dispersion of pollutants in freshwater ecosystems is EXAMS, the Exposure Analysis Modeling System developed by EPA. Alternative models that could be useful in specific cases are TOXIWASP and SLSA (see Section VI.C.1).

(2) Preferred watershed models: The selection of a watershed model is more arbitrary than selection of other transport models. Availability of adequate data, particularly hydrologic and soil erosion data, is a common limitation. Selection is often dictated by matching data needs with data availability and comparing site characteristics with model capabilities (see Chapter VI). Model selection can be made only after these environmental factors and chemical and physical processes have been addressed. Validation of runoff models is difficult.

The recommended model for predicting transport of hazardous waste pollutants from watersheds is HSPF, the Hydrological Simulation Program-FORTRAN. It is a simulation model that incorporates two runoff models (ARM and NPS) and an in-stream transport model (CMRA) (see Section VI.C.2). It provides a comprehensive analysis framework that can also yield estimates of acute health risks if inputs are made of LD_{50}s or MACs for toxicants.

c. Air dispersion and deposition models: A very large number of air models are available. Models considered appropriate for a generic methodology were: (a) those approved by EPA and included in the User's Network for Applied Modeling of Air Pollution (UNAMAP-4) series; and (b) the Atmospheric Transport Model developed by Oak Ridge National Laboratory and considered a "reference" model in the OAQPS Guidelines Series. Based on the review in Section VI.D, recommended models are:

- Industrial Source Complex (ISC) in either its short- term or long-term versions (ISCST or ISCLT) was rated one of the most useful models in the UNAMAP series for area source application involving hazardous waste TSDFs. The ISCLT has the analytical capability to simulate the plume depletion and particulate deposition processes likely to be essential for modeling emissions from many long-term hazardous waste operations. It is currently being used as the concentration modeling component in the Inhalation Exposure Modeling (IEM) system. The ISCST is particularly useful for short tests (e.g., trial burns in hazardous waste incineration) and for analysis of the effects of malfunctions and system upsets.

- Atmospheric Transport Model (ATM) has several features that make it potentially useful for dispersion modeling of toxic pollutants. It has analytical capabilities similar to the ISCLT to simulate the plume depletion and particulate deposition processes, but was judged more useful in point source applications. A modified version of the ATM called ATM80 is preferred. The ATM is a component of GEMS (see multimedia models, below).

- Gaussian Plume Dispersion Algorithm (VALLEY) of the UNAMAP series is recommended (despite its limitations) for applications involving complex terrain at the source. Improved models should be considered as they become validated.

d. Multimedia models: Multimedia models are in an early stage development. Based on the review in Section VI.F, recommended models are:

- Graphic Exposure Modeling System (GEMS) is a comprehensive, multimedia model system developed by EPA's Office of Toxic Substances. It integrates selected single media models. It is particularly useful for air-related transport (it uses the ATM for the air dispersion component).

- Unified Transport Model (UTM) and its organic chemical version, UTM-TOX, combines selected models in series to give multimedia capability, particularly in the water-related transport. Data needs are extensive.

e. Uncertainties: Prediction of environmental transport and fate of contaminants are subject to uncertainties from several causes including: deficiencies in input data; selection of optimum model for a given aspect; inherent deficiencies in the models selected; and difficulties in linking selected models. Data deficiencies are expected routinely. Of the available models, validation of some of the air and water dispersion models appears adequate, but validation efforts for watershed runoff and groundwater models is just beginning for nonreactive pollutants; reactive pollutants are modeled less confidently. Data limitations can determine model selection to a significant extent. Uncertainties arising from linking transport models have not been studied extensively, but are not believed to be significantly larger than uncertainties in the models themselves.

C. Exposure Prediction

Exposures must be predicted for two key human population categories: (a) workers who are directly involved in activities involving hazardous wastes; and (b) members of the public who may come into contact with contaminants released from hazardous waste TSDFs and transported through environmental routes. In addition, exposure predictions can be required in comprehensive risk assessments for natural and domestic populations of plants and animals, and for other objects of economic or aesthetic value. For each category the exposure prediction requires three analytical activities:

- Qualitative identification of population groups likely to be significantly exposed.

- Quantitative estimation of the number of individuals in each group.

- Quantitative estimation of the magnitude of exposure of each group.

Available methods and resources for predicting populations exposed and magnitude of exposures are reviewed in Chapter VII. Quantitative exposure prediction requires characterization of many modifying factors as suggested by the checklist in Table IV-3 for human exposures. The discussion below addresses methods only for workers and the public, and focuses on exposures that may cause adverse health effects. Many of the concepts are also applicable, however, to prediction of exposures for nonhuman receptors.

TABLE IV-3

CONSIDERATIONS IN CHARACTERIZING HUMAN EXPOSURE TO CHEMICALS FROM HAZARDOUS WASTE MANAGEMENT

Pollutant Profile	Population Profile	Immediate Sources of Exposure	Exposure Parameters
Media	Distribution	Drinking and bathing water	Route
	Geographical		Inhalation
Chemicals	Numerical		Ingestion
		Food crops	Absorption, skin
Concentrations	Nature		
	General	Nonfood products used in daily life	Intensity
Change with time	Special		
			Frequency
	Change with time		
		Indoor air	Duration
		Ambient air	
		Lifestyle activities	

1. Exposed workers: Work practices at existing or future hazardous waste TSDFs must be analyzed on a case-by-case basis in order to identify those workers likely to come into contact with toxic or otherwise hazardous substances, either through normal activities, accidental events, and corrective/remedial actions, such as spill clean-up, leak repair, or groundwater recovery/treatment. The assessment must identify the types of workers exposed, the number of each type, and the frequency, intensity, and duration of exposure to all relevant toxicants, including any chemicals that may be used to treat the hazardous waste before disposal or used in remedial actions. Worker exposures tend to be work-station specific; the first activity, therefore, is to characterize the number of different types of work stations and the number of workers at each.

Exposures are difficult to estimate quantitatively if monitoring data are unavailable. The primary route of exposure is most often by inhalation, but absorption through the skin, and hand-to-mouth transfers are also possible. Exposures will vary with the chemical and physical nature of the materials being handled, the technology being used, and control measures and training programs in place. They will also vary with the individual's use of available control measures and prescribed practices (e.g., use of dust masks). In general, estimation techniques are relatively crude for predicting worker exposures around TSDFs. Well-validated mathematical models are not available.

Secondary exposures of worker's families can be considered; they are extremely difficult to quantify confidently, however, unless very good monitoring data are available.

Occupational exposures are aggregated in subgroups by type or source of exposure (e.g., chemicals, work station, route, etc.), and summed by magnitude of exposure (intensity, frequency, duration), as appropriate for subsequent use in the health effects prediction. In some comparative risk assessments, qualitative estimates of worker exposures might be quite sufficient as an input to decision making, because public health concerns may predominate. In other cases, quantitative estimates may be needed for both the average worker exposure and for the maximally exposed worker. Special note should be made of any predicted levels that are above regulatory standards for short-term or long-term exposures.

2. Exposed public: Predicting exposures of members of the general population to environmental contaminants from hazardous waste TSDFs requires consideration of where the contaminants and the people intersect in space and time. Exposure routes that must be considered include inhalation of contaminated dusts, mists and vapors, ingestion of contaminated water, food, beverages or other substances, and dermal absorption following contact with contaminated substances. In some cases, environmental monitoring data may be available that define contaminant levels at the point of contact with humans. In general, however, a major input to this analysis will be the output information from the modeling of environmental transport and fate of the chemicals in relevant media after they leave the TSDF site. In some cases attention must also be given to transportation accidents that would cause additional point (or possibly nonpoint) sources. In either case, the analysis will have provided information on the spread (both geographically and over time) of the pollutants from the source through the air, surface water, groundwaters, and other environmental compartments. Exposure prediction will require profiles of the exposed population and exposure conditions and integration over populations and conditions.

a. Population profiles: In most assessments the chance of exposure will depend primarily on where people live, but it can also depend on where they work (i.e., jobs unrelated to TSDFs) and on other lifestyle factors that would increase exposure. A second major input will therefore be demographic information on the distribution of potentially exposed populations in the contaminated areas. If appropriate in a given assessment, distribution of jobs, day schools and other relevant lifestyle activities can be determined around a particular site. In addition to private homes, residents of hospitals, nursing homes, and boarding schools should be considered.

A detailed population profile is then developed, based on the geographical boundaries determined for the pollutants' dispersion through air and water away from the sites of hazardous waste disposal activities. Specific coordinates are desirable in defining the study area sectors, since several data bases, including that of the U.S. Bureau of Census, can correlate their data by latitude and longitude. In the U.S. Census data, population enumerations are broken down by urban and rural areas, age, race, sex, commuting patterns, and household data. All data can be related to geographical coordinates. Only at the urban block level, however, can a relatively small group of people (~ 70) be related to a relatively small area (one city block). Coordinates of larger rural Enumeration Districts (~ 4,000 people) represent the population center for the designated area. Because pollutants follow natural patterns rather than political and statistical boundaries, the Census enumerations will often have to be split to develop the population profile.

Some models contain programs that access population data bases directly. For air pollutants, dispersion of the plume over residential areas and resultant inhalation will be of major concern. Using GEMS, the ATM dispersion model can be coupled with the Sector Population (SECPOP) program to retrieve 1980 census data. The model then calculates the average annual concentration and exposed population for directional sectors radiating from the emission sources. Inhalation at site-specific commercial or institutional facilities can require additional consideration in some cases, and alternate exposure routes (such as deposition of pollutants on foods or surfaces) may require attention in others.

For pollutants entering groundwaters or surface waters, additional information will be needed to supplement the Census data. For example, the location of public and private drinking water supplies will have to be pinpointed relative to the pollutants' dispersion. Information on most community water systems can be obtained from EPA (Federal Reporting Data System) and information on privately owned wells and springs from the U.S. Geological Survey's Groundwater Site Inventory. Additional information may be available from state or local agencies for a specific site. Populations potentially exposed by ingestion of drinking water should then be identified. Populations that would consume foods or beverages prepared from the water should also be identified if they are significantly different from those drinking it, e.g., customers of a commercial food processor or beverage bottler that uses the water. For some pollutants absorption through the skin during bathing or other contact and inhalation of chemicals volatilizing in the shower may require consideration.

In some assessments, nonresidential and lifestyle factors will need to be considered. For example, persons that commute daily through a dispersion plume or frequent recreational activities in potentially contaminated lakes or parks may need to be considered. Specific information on the dynamcis of the subpopulations within the area of interest can often be obtained from local governments or planning commissions. A preliminary analysis of the geographical distribution and population distribution can then determine the major exposure routes and specific locations where the general population densities should be modified for the supopulations.

Uncertainties in identifying the general exposed population will depend on the quality and completeness of the data available, but should be small compared to those in other steps of the risk assessment. Uncertainties will be greater in trying to quantify supopulations for detailed exposure analysis, either because of difficulty in specifying the subpopulations or in obtaining geographically coded information.

b. Exposure profile: An exposure profile must be developed for each of the identified exposed population groups. This profile should identify three chaacteristics of the exposure:

- Route of exposure: air, water, foods, soil, or other routes
- Time over which exposure will occur: time to onset and duration
- Concentration of contaminant received: concentration by route and variation over time

Appropriate models or other estimation techniques are used. In many cases, estimates will be needed for the average exposures for residents in an area, for the maximally exposed resident, and for especially sensitive subpopulations as discussed in the next subsection.

c. Exposure integration: The exposure integration process involves aggregating exposure to the extent possible over routes, concentrations, time, and population groups. The degree of aggregation that is reasonable can depend on several aspects of the contaminants. The toxicological properties of the chemicals of concern will be particularly important, but physical-chemical properties and route of exposure may also require consideration.

Aggregation across exposure routes and concentrations should usually be straightforward unless many subpopulations have been identified. The simplest case would involve one population group uniformly exposed to a constant concentration of contaminant, e.g., in the air breathed or drinking water consumed. In cases where exposure to the chemical by different routes is likely to have different effects, aggregation across routes should be avoided. In cases where a wide range of exposure levels occurs that are likely to have different effects, aggregation should be avoided.

Aggregation across population groups can be more difficult. If exposures vary widely across groups, the "most exposed" groups or individuals (MEIs) should be identified. They generally should not be aggregated with all other groups to calculate an average or mean exposure level, because most of the adverse health impacts could be incurred by a small number of highly or frequently exposed persons. Bounding between MEIs, less-exposed populations, and populations with de minimis exposures is desirable.

Aggregation across time also requires care in that some health effects are associated primarily with short-term exposures at relatively high concentrations, while others are associated with long-term (even lifetime) exposures at lower levels. Population groups with substantially different temporal aspects of exposure (e.g., short vs. long term; intermittent vs. continuous) should be treated separately in the health effects estimation and should not be aggregated in the exposure prediction.

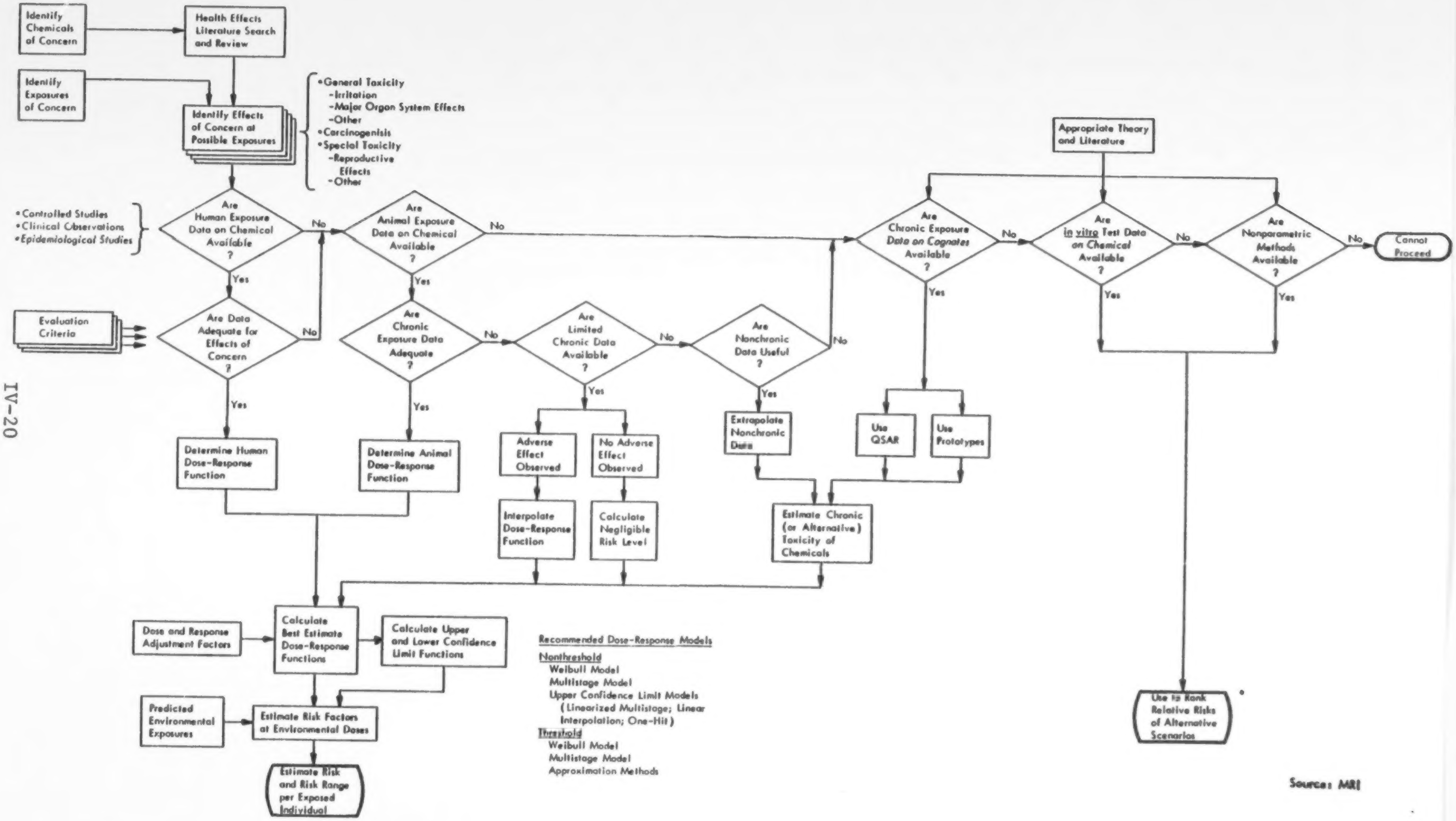
In summary, the integrated exposure assessment tabulates all significant population groups according to the relevant environmental dose that each is estimated to receive.

D. Health and Environmental Effects Analyses

The toxic and environmental properties of the pollutants of concern will have been partially determined in Step 1, Source Assessment. Information on these chemicals must now be assembled, evaluated, and converted into forms that will be useful for predicting the health and environmental effects of estimated exposures of future populations. Specific activities will include: review the health effects literature for the specific chemicals; identify the kinds of responses likely and of concern in the expected exposure range; develop dose-response relationships covering the range of exposures; and develop risk factors for specific environmental doses for exposed individuals. Figure IV-3 shows schematically the relationship of these activities and outlines the procedure (to be discussed below) for selecting the generally best available data for developing the dose-response models. The several elements of this schema are discussed below in terms of assessing human health risks, but many of the elements would be similar for assessing health impacts on other species. Chapter VIII provides an extended discussion (with references) of the theoretical aspects of health effects prediction approaches.

1. Evaluate available literature: A thorough search for and review of the literature describing the biological effects of the chemicals of concern is made.

a. Search scope: The scope of the search should include all chemicals likely to be present in relatively high concentration at point of exposure and other chemicals that have special toxic or environmental properties. The full range of health effects will be of interest in the assessment. A given chemical of concern may produce a variety of effects depending on exposure conditions. In many cases, the researcher will be able to focus on one or two of the most significant effects, particularly any irreversible ones likely to occur from low dose, long-term exposures through environmental routes. If exposures are apt to be widely variable over time, however, effects of acute exposures may also require consideration and may even predominate in the assessment (e.g., if a spill of a concentrated toxicant might occur). In general, the most significant concerns will be carcinogenesis, reproductive effects (including mutagenic, teratogenic, and fertility effects), and any effects associated with bioaccumulation. If the literature search does not develop adequate data on the chemicals of concern to apply preferred estimation methods, it may be necessary to expand the search to include selected similar chemicals so that less preferred methods may be attempted.


Identify Chemicals of Concern
Health Effects Literature Search and Review
Identify Exposures of Concern
Identify Effects of Concern at Possible Exposures
•General Toxicity
-Irritation
-Major Organ System Effects
-Other
•Carcinogenisis
•Special Toxicity
-Reproductive Effects
-Other
•Controlled Studies
•Clinical Observations
•Epidemiological Studies
Are Human Exposure Data on Chemical Available ?
No
Yes
Evaluation Criteria
Are Data Adequate for Effects of Concern ?
No
Yes
Determine Human Dose-Response Function
Are Animal Exposure Data on Chemical Available ?
No
Yes
Are Chronic Exposure Data Adequate ?
No
Yes
Determine Animal Dose-Response Function
Are Limited Chronic Data Available ?
No
Yes
Adverse Effect Observed
No Adverse Effect Observed
Interpolate Dose-Response Function
Calculate Negligible Risk Level
Are Nonchronic Data Useful ?
No
Yes
Extrapolate Nonchronic Data
Estimate Chronic (or Alternative) Toxicity of Chemicals
Appropriate Theory and Literature
Are Chronic Exposure Data on Cognates Available ?
No
Yes
Use QSAR
Use Prototypes
Are in vitro Test Data on Chemical Available ?
No
Yes
Are Nonparametric Methods Available ?
No
Yes
Cannot Proceed
Use to Rank Relative Risks of Alternative Scenarios
Dose and Response Adjustment Factors
Calculate Best Estimate Dose-Response Functions
Calculate Upper and Lower Confidence Limit Functions
Predicted Environmental Exposures
Estimate Risk Factors at Environmental Doses
Estimate Risk and Risk Range per Exposed Individual
Recommended Dose-Response Models
Nonthreshold
Weibull Model
Multistage Model
Upper Confidence Limit Models
(Linearized Multistage; Linear Interpolation; One-Hit)
Threshold
Weibull Model
Multistage Model
Approximation Methods

Source: MRI

Figure IV-3 - Schema for Selection of Health Effects Estimation Models Depending on Availability of Data

b. Literature search: Literature search techniques will depend on how well-known (or how obscure) the chemicals of concern are. Many commercial compounds and some newer chemicals have been subjects of much recent study. A well-evaluated review or summary document may be available, such as those produced by EPA (e.g., a Criteria Document or an analysis by the Carcinogen Assessment Group), the National Academy of Sciences, the National Institute of Occupational Safety and Health, the National Institute of Environmental Health Sciences, or the International Agency for Research on Cancer. Such reviews may eliminate the need for further intensive evaluation or reduce the literature search and review to significant new publications. In other cases, computerized or manual searches of the original literature may be required so that key studies can be identified for evaluation. (Computerized searches will be quicker; both can sometimes miss important documents.) Primary information and data sources will include controlled toxicological studies, clinical observations or epidemiological studies on humans; acute, subchronic, chronic, and special toxicological testing with laboratory or domestic animals; toxicological tests with microorganisms; and any pertinent biochemical tests.

c. Judging quality of data: A key point in the risk assessment is the decision whether or not a particular study is acceptable as a primary basis for the analysis. This may at times be a partially subjective judgment, and it is important to have acceptability guidelines that are as objective as possible. Data that are not fully satisfactory may have to be used sometimes in the absence of adequate data, but deficiencies in the data will affect the uncertainty in the risk estimates and must be noted. Important checkpoints of the acceptability guidelines for human and animal data are listed below.

d. Human studies: The conclusions from even good quality human studies can be less certain that those from animal studies because of the number of potential confounding factors. Points to watch include:

- The study (exposed) population should be carefully documented as to source and characteristics.

- The control (unexposed) population in analytical epidemiological studies or reference population in descriptive epidemiological and clinical case report studies should be documented and described.

- The sample size of the study and control populations should have been sufficient to meet statistical criteria. Potentially confounding factors such as age distribution, sex, and lifestyle (particularly smoking and use of controlled substances, if known) should be controlled in the study design.

- The study population should have been exposed to as few toxicants as possible -- preferably just the chemical of concern -- and to a minimum of other variable stresses.

- Exposures should have been quantified. The exposure assessment should be documented. Preferably, data will be available from appropriate sampling and analytical monitoring at the point of exposure or in bodily fluids or tissues. The duration and time sequences of exposures should be noted.

- Source of response data should be documented. All clinical signs should be reported. The length of the follow-up period should be reported so that latent effects, if any, can be properly evaluated.

- The response of the control population should have been similarly studied, particularly for effects of chronic exposures.

- Statistical analysis should have been made, consistent with the study design. Causal associations between exposure and response should have been inferred only if chance, bias, and confounding factors have been ruled out as explanations.

- One or more dose-response relationships should be evident in the data, and any effects of other variables should have been reported.

e. Animal studies: Points on which to judge the quality of animal studies include:

- The number of animals of a given study should be adequate. In a chronic study, there should be 50 or more animals per dose group for each sex. In a teratology study, there should be 10 to 12 female rabbits or 20 or more female rodents per dose group. If one is particularly interested in effects at low dose, studies using larger numbers of animals are highly desirable, although generally not available.

- There should be at least three dose levels (depending on the type of study) in addition to the controls. The highest dose level should produce some toxic symptoms but not cause more than 10% unscheduled deaths. The lowest dose, ideally, should produce essentially no toxic symptoms.

- There should be an untreated control group and its number should be the same as that of the test group. This group should have received vehicle doses if one is used for compound administration.

- The route of administration should be the same as the expected exposure route for humans.

- There should not be an excessive number (> 10%) of "diseased" animals or early deaths in the control group, especially if the lesion is similar to or the same as the lesion observed in the treated group. The response of the treatment groups should be dose dependent.

- All major organs should be listed in the pathology tables. This is a measure of the quality of the study. Failure to note numerous organs can be an indication of poor necropsy or tissue processing techniques.

- Any clinical signs, such as anorexia, alopecia, or conjunctivitis, should be listed in tabular form. The same should be true for clinical chemistry and hematology data when these are part of the study.

- All studies should have supporting dose analysis data and chemical methodology to ensure quality control. (These are least critical for acute exposure studies.)

- A dose-response relationship should be evident in the data.

- Peer review comments, if available, should be closely examined for possible shortcomings in the study.

- A study's materials and methods section, the seldom explicit "untoward results" section, and the conclusions section, should be carefully read to evaluate it.

In practice, the risk assessment team will find toxicity studies that satisfy all of these criteria are available for few chemicals. It should take any deficiencies into account in the uncertainty analysis.

2. Identify likely responses: The literature review generally will have revealed that the chemicals of concern cause one or more adverse responses in test organisms under one or more conditions of exposure, or would be likely to cause adverse effects in exposed humans. The full range of effects that might result from potential exposures will be of some interest, but the final identification of effects to be assessed will depend on the significance and quality of the reported data and on the likelihood of response at predicted exposures.

Studies reporting general toxicity effects based on acute or subchronic exposures are analyzed first if they are available. In many assessments, fairly high level exposures in occupational activities or from accidental releases might be of concern, and information on responses under these conditions will be needed. Of greater priority in most assessments of hazardous waste management alternatives, however, will be any serious irreversible effects that could result from exposures in the range of those actually predicted. In particular, one should identify effects on major organs or systems resulting from low level chronic exposures, and carcinogenic, genetic, and reproductive effects that might occur under a range of exposure conditions. In general, data from one or more chronic exposure studies are highly desirable, and data from human studies would be preferable to data of comparable quality from animal studies, as was indicated in Figure IV-3. If data from appropriate human or animal studies are not available, then one resorts progressively to less preferable methods that involve greater extrapolations or assumptions. Cross-checks between one or more of these alternative methods should be made, where possible, to improve the prediction of the kinds of effects.

Information on the dose-response patterns for potential effects of a chemical is compared with predicted exposure patterns to identify those effects likely to occur at estimated environmental exposures. Graphical plots of the original data, if not already provided, will be helpful, particularly when several studies are available. One may be able to omit effects likely to be found only at very high acute exposures if only low level exposures are possible, but caution must be exerted at this point not to discard information that could be useful in a subset of the assessment (e.g., a catastrophic release). Studies showing positive response in humans would be given greater weight than negative studies in lower mammals; studies showing positive response in short-term microbioassay or rodent studies but not in higher mammals are difficult to generalize since the quality of the specific data and the toxicological principles involved are critical. If the chemical has special toxicity (such as carcinogenicity or reproductive effects), low dose exposures always will be of concern.

The effects can usually be identified with reasonable confidence if toxicological test data in animals or other organisms are available for the test chemical or for cognate chemicals (i.e., other chemicals with similar chemical structure and physicochemical properties), or if toxicokinetic (pharmacokinetic) information on the chemicals' absorbability, mobility, and biotransformations within the human body or other appropriate species are available.

3. Develop dose-response relationships: Dose-response relationships must be developed for the most significant kinds of effects identified in the preceding section. All the available data should be considered in developing the most reliable dose-response model in humans for each significant effect of each chemical being assessed under the exposure conditions predicted. Ideally, a quantal dose-response relationship will be available that can be expressed graphically and mathematically.

The procedures used in developing the dose-response relationship will depend on the nature of the available data, toxic effect, and the assumptions and extrapolations that must be made for predictive purposes. The procedures in each case are outlined below.

a. Data preference: If adequate dose-response data are available from studies of human exposure to the chemical of concern, they can be used directly to calculate the dose-response function using an appropriate mathematical model. The dose-response function based on the literature data is then applied (after appropriate conversion of dosage units, if necessary) to the estimated actual exposure from the hazardous waste disposal activity to give an estimated risk factor for an exposed individual or population.

If data on humans are not available, the animal data are the next choice. Any available toxicokinetic data that are available should be considered. If chronic animal test data are available and adequate, the same appropriate mathematical model is used as with human data for dose-to-dose interpolation and extrapolation as above. If chronic animal data are limited, but are indicative of an effect, a simpler model still might be useful in estimating the risk approximately. If chronic studies were made but no adverse effects were observed, these data can be used to calculate an upper limit risk level.

If no chronic studies have been made, less accurate methods are used. In some cases nonchronic exposure data on animals are available that may be useful in estimating effects of chronic exposures. Extrapolation of the results from short-term studies to long-term exposures is a difficult step because, among other problems, some effects (e.g., carcinogenesis) are seen only in longer term studies. Therefore, this type of extrapolation should be done only if absolutely necessary (see Section VIII.B.1).

If chronic test data on several cognates are available, quantitative structure-activity relationships (QSAR) may be used to estimate the chronic toxicity of the chemical of concern relative to the cognate. If nonchronic exposure data are available for the chemical and similar data plus chronic data are available for one or a few prototypes, their relative dose-response functions can be used to estimate chronic toxicity of the chemical. If data on cognates are unavailable but nonchronic exposure data are available for the chemical, these are extrapolated approximately on the basis of general toxicological principles, if possible, to estimate chronic toxicity. Finally, ranking methods are used as a last choice to compare the health risks of alternative decisions if no methods are available for generating numerical estimates. Rankings are based on the use of in vitro test data on the chemical or the use of nonparametric methods [see Section VIII.B.2.c.(6)].

The uncertainty associated with estimates from these alternative methodologies will be greater than with the primary method, and perhaps by two extra orders of magnitude or more in addition to other uncertainties.

b. Threshold and nonthreshold effects: A decision must be made on whether the dose-response function should be developed with a threshold dose or as a nonthreshold model. This decision generally cannot be made strictly from the observed dose-response data, but must be made on theoretical grounds.* While thresholds were once believed inherent in biological response to disturbing stimuli, nonthreshold models of cancer gained substantial acceptance over the past 40 years. More recently, nonthreshold models have been proposed for several other effects involving molecular biology and genetics, and even for some effects previously presumed widely to have thresholds (e.g., brain damage from lead; teratogenic effects). The present methodology assumes that many chemicals will exhibit systemic effects for which a threshold model is appropriate and that other chemicals will exhibit carcinogenic or other effects for which a nonthreshold model may be demanded.

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* See discussion in Section VIII.A.3. In some instances, the analyst may wish to estimate risks by both threshold and nonthreshold models for comparison.

(1) Nonthreshold model: For health effects that are assumed not to have dose thresholds, nonthreshold versions of the multistage and Weibull models are used. The EPA has adopted the "linearized" multistage to estimate upper confidence limits on risk and lower confidence limits on "virtually safe doses" for numerous carcinogens; EPA's Carcinogen Assessment Group has developed substantial documentation with this method in support of regulatory decision making. The CAG method is therefore adopted here to estimate the model-based upper confidence limit on risk as part of the uncertainty analysis. Best estimates of the risk are then also made using either or both the Weibull model or the conventional multistage model. Use of these models is discussed below.

The Weibull model is usually an excellent choice for making risk extrapolations to very low exposures, provided the available data sets are not deficient in dose groups in the mid and low dose range. For data sets with conventional spread and shape, the Weibull generally yields: a good fit to data points (even if the data have a threshold-like appearance); a low dose extrapolation that is nearly linear; and risk estimates that are near the average for those of several other models used (i.e., intermediate between those of the one-hit and multistage models on the high risk side and those of the logit and probit on the low risk side).

The biological rationale for the Weibull (once considered a weakness) has been expanded to a point [see Section VIII.B.2.a.(3)] that it appears to be of comparable stature to that of the multistage (it has fewer introduced constraints than the multistage and linearized multistage*). If the data set lacks a dose group in the low response range, the multistage model may provide a better representation of the probable dose-response relationship and can be used. (Alternatively, both models can be employed and a geometrical average taken for the risks estimated at predicted exposures.)

The time-independent form** of the Weibull model is expressed by the equation:

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* R. E. Albert, Chairman of EPA's Carcinogen Assessment Group recently noted that an overall feeling exists that the biological foundation is flimsy for EPA's current method of low level risk estimation [see Section VIII.-B.2.a.(3)].

** A general form of the Weibull distribution is:

$$P(t,d) = 1 - e^{-(\alpha + \beta d^{m})(t - w)^{k-1}}$$

where t is the time after dosing starts, w is tumor growth time, and k is a number of discrete changes leading to tumors.

$$P(d) = 1 - e^{-(\alpha + \beta d^m)}$$

where P(d) is the probability of response at dose d and α, β, m are parameters to be estimated ($\beta, m > 0$). Alpha (α) is determined by the background incidence; β, a scale parameter, depends on the units of dose; m is a nonnegative shape parameter, not necessarily an integer, and usually in the range 1 to 5. The low dose extrapolation is linear if $m = 1$, convex if $m > 1$, and concave with $m < 1$. A value $m < 1$ may reflect an absence of sufficient low dose data points or the existence of unusual toxicokinetic features of the substance: comparison with results from the multistage would be desirable in this case.

If the background incidence is neglible ($\alpha \cong 0$), or if one wishes to express the extra risk over background, then the Weibull expression becomes:

$$R(d) = 1 - e^{-\beta d^m}$$

where $$R(d) = \frac{Pd - P(d_o)}{1 - P(d_o)}$$

The multistage model expresses the probability of response upon continuous lifetime exposure at dose, d, by the equation:

$$P(d) = 1 - e^{-(\beta_0 + \beta_1 d + \beta_2 d^2 + \ldots \beta_k d^k)}$$

where k = an integer, nominally the number of stages in the process, and

β_n = nonnegative parameters to be estimated from the data set.

If the background incidence is zero, then $\beta_0 = 0$ and the equation at low dose is:

$$P(d) = 1 - e^{-(\beta_1 d + \beta_2 d^2 + \ldots \beta_k d^d)}$$

For some minimal data sets, interpolation between the lowest dose data point and the background point or use of the one-hit model may be necessitated. Both the Weibull and the multistage models contain the one-hit model as a special case, obtained by fixing m or k respectively equal to one. The one-hit model equation is:

$$P(d) = 1 - e^{-\beta d}$$

where βd = expected number of hits at dose, d. The model can be used with any positive response data even if only one useful data point is available, because, for purposes of rough estimation, the slope of the curve can be assumed. Linear interpolation between the data point and the origin or background gives essentially the same slope; both probably overestimate the risk at very low dose. A combination convex-linear interpolation (see Section VIII.A.3) can be used for a best estimate.

The modeling procedure is generally as follows. After the experimental data are assembled and evaluated, the appropriate mathematical model is fitted to each selected data set by regression analysis. Several computer programs are available for the Weibull [see Section VIII.B.2.a.(3)]. The GLOBAL 83 program for the multistage (accessible from the National Institutes of Health, Bethesda, MD) determines the number of necessary terms in the polynominal exponent, the coefficients of each, the goodness of fit (chi-square statistic) of the model to the data, the probability of response to any given dose (or the extra risk if a background exists), and the dose that poses a given risk. The maximum likelihood values of the coefficients are needed; upper confidence limits can also be obtained for subsequent sensitivity analysis.

If the models do not fit all the data sufficiently well, it may be because one or more high dose responses are anomolous (e.g., the curve bends downward because subjects die of other causes. If this appears to be the case, the highest dose point is deleted and the model is refitted to the rest of the data. If the fit is still inadequate, the next highest dose points could be deleted in order; a fit will always be obtained for the lowest dose point and the control. Practical judgment should be exercised, however, so that reproducible midrange data points are not discarded in favor of a possibly anomolous low dose point.

The goodness-of-fit test used is a chi-squared comparison of the actual data points with the estimated effects at the same doses on the calculated regression curve.* A cumulative chi-square over 99% is considered unacceptable. High values of the test indicate a poor fit. Goodness of fit of the regression curve alone is not a determining factor in rejection of results, of a model, or of statistical correlation inferences.

When all the regression calculations are complete and evaluated, one or more curves should be available from which to estimate the probability of each adverse effect of each chemical for exposed populations. If multiple data sets are available and are of comparable quality, the probabilities at a given dose can be averaged geometrically.

(2) Threshold model: If the dose-response relationship is believed to have a threshold dose, a threshold version of either the

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* The chi-square statistic is discussed with the linearized multistage model in Section VIII.B.2.a.(3).

Weibull or multistage mathematical model is used. The Weibull model is generally an excellent choice because of the limited number of variables and generally good flexibility in fitting data sets. The equation is:

$$P(d) = 1 - e^{-[\alpha + \beta(d - d_t)]^m}$$

where d_t is the threshold dose to be provided and α, β, and m are variables determined by regression analysis. The multistage model may be preferable if the data set is deficient in the mid and low response range, but may be undesirable if the curve rises rapidly and then plateaus [see Section VIII.B.2.-a.(3)] for further discussion). The threshold version of the multistage model is:

$$P(d) = 1 - e^{-(\beta_0 + \beta_1(d-d_t) + \beta_2(d-d_t)^2 + \ldots + \beta_k(d-d_t)^k]}$$

where d_t is the threshold dose. For either model, the risk is zero for exposures below the threshold dose. Above the threshold, the risk can be determined directly from a curve fitted to the experimental data or from the model.

The identification of the threshold dose to be used is usually a problem. The available data are often for continuous or graded responses, and quantal data can be difficult to interpolate because of the normal asymptotic approach of the dose-response curve to the base or background line.

Acceptable daily intakes (ADIs) will have been established for many chemicals based on the application of an appropriate safety factor to a no-observed adverse effect level (NOAEL) or lowest observed adverse effect level (LOAEL) in experimental data. The risk is assumed to be zero at the ADI, at least for almost everyone. The threshold dose itself is assumed to be well above the ADI, but below any LOAEL. The precise number is usually rather uncertain, even if a NOAEL is reported. For predicted exposures that happen to be in the threshold dose region, the estimated risk is highly sensitive to small changes in dose and to the assigned threshold number. In the interest of consistency in assessing risks when definitive data are lacking, the following three-tier process is suggested:

- If an ADI has been established, the risk is assumed to be zero at it and up to the threshold defined as 5 times the ADI. The value of 5 is not based on any regulation, but appears to be a reasonable choice, based on the practice of dividing a NOAEL by a safety factor of 10 (or more) to obtain an ADI, a practice based on toxciological and public health experience. In the unlikely event that the experimental data show an adverse effect at the 5 times ADI level, a smaller multiple should be used. This threshold dose is then used in the Weibull (or multistage) model.

- If an ADI has not been established, the threshold dose is determined from the NOAEL(s) if one or more is reported. The threshold can generally be taken as 1/2 of the most relevant NOAEL, but a smaller fraction could be appropriate depending on the nature of the data, as in the safety factor concept. (Note that this is a threshold for risk assessment, not an ADI for regulatory purposes.)

- If neither an ADI nor NOAEL are available, the threshold dose is determined from the LOAEL(s) in the available data. The LOAEL is multiplied by a fraction commensurate with the nature and quality of the experimental data. A fraction of 1/10 should be appropriate for most data sets, but smaller fractions (e.g., 1/100) may be required in others. (Note again that these are estimated thresholds, not ADIs.)

The uncertainties in model-estimated risks should be analyzed. Confidence limits should be determined in the experimental range from the data or fitted model and in the low-dose extrapolation. (Note that these are model-dependent confidence limits.) If information indicates that especially sensitive persons may be at risk at the population threshold or even at the ADI, this should be noted.

c. Adjustment factors: A number of assumptions and conversions may be needed in order to be able to predict the degree of the effect of concern at expected exposure conditions based on the different set(s) of exposure conditions reported in the studies found in the literature. These predictions almost inevitably will require the extrapolation of a dose-response function across two or more sets of conditions. These include extrapolations across: exposure routes; temporal conditions (frequency, continuity, duration); species; dosage units; and from toxicological test data on individual chemicals to the exposures to complex mixtures of chemicals frequently found in hazardous wastes. All of the available data should be considered in a given case, but defensible default positions are listed below.

(1) Exposure routes: The default assumption is that the effects of exposures by oral and inhalation routes are equal, with absorption assumed to be 100% by both routes. If different assumptions are warranted by information on the chemical of concern or actual exposure conditions, adjustment factors should be developed and explicitly stated. For example, the bioavailability of a chemical can vary with the medium it is in. Dermal absorption rates tend to vary greatly with the chemical and its carrier, if any, and must be estimated on a case-by-case basis. Simultaneous exposures by multiple routes are assumed to be additive (within the above guidelines), unless an adjustment factor is indicated.

(2) Exposure variation over time: Exposures can vary in frequency, continuity, or duration between the studied population or species and the population subject to analysis. The default assumption is that variable exposures have roughly the same effect, if the total dosage is

equivalent. If total dosage differs because of such variations, the effect is assumed to be comparable on a prorated (time-weighted average) basis. For reversible acute effects, the peak exposure dose is of primary significance, but time-weighted averages are required for other doses. If warranted by information on the chemical of concern or exposure conditions, adjustments should be made. For example, intermittent exposures may be nearly equivalent to continuous doses if the chemical is strongly retained or may be nearly without effect if it is rapidly excreted.

If the conditions of exposure differ significantly between test and subject population, all available data should be considered in developing adjustment factors and in estimating the uncertainty of the results. Prorating such factors require special care when extrapolating chronic test data to short-term (even single) exposures of the subject population to carcinogens. Special care is similarly required when extrapolating minimal chronic test data to lifetime human exposures, especially if the chemical bioaccumulates, if the chemical is a suspect carcinogen on other grounds, or if the body develops a tolerance to it. The analysis tends to become chemical specific.

(3) Animal to human extrapolation: The default assumption is that the effects of a given dose are the same in humans as in test animals at equivalent doses (see "units" below). If there is clear evidence in a given case that this assumption is inaccurate, then an appropriate adjustment factor is used in estimating risk.

(4) Exposure units: The human exposure levels reported in epidemiological studies or test dosages in animal studies and the anticipated environmental exposures are converted to consistent dose units for comparison. Appropriate units are: milligrams per square meter (mg/m^2) of body surface area of the species per day exposed, for most toxic effects;* mg/m per pregnancy** for teratogenic effects; mg/m^3 for effects of acute inhalation exposures; and concentration in carrier (e.g., mg/mL) for acute irritation effects. If the test data are reported in terms of dose per unit weight (kg), the conversion factor used for interspecies is: $m = 0.106(kg)^{2/3}$.

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* These are the units currently preferred by EPA. The more widely-used units milligram per kilogram (mg/kg) of body weight give lower estimates of absolute risk. In many assessments the comparative risks will be insensitive to the units used since exposure to the same chemical(s) will occur under all waste management alternatives.

** Female test animals (mice and rats) may be dosed over either the entire gestation period or on just 1 to 7 days of their sensitive periods which is about one-third of the total gestation. Total dose per pregnancy is a convenient test statistic that would, at worst, overestimate, by a factor of three, the effect of human exposure to the same dose (i.e., in a case where the dose was received entirely during the sensitive period). It would generally be more accurate for low level environmental doses.

Standard weight and intake factors are assumed for all species. Reference man weighs 70 kg, consumes 2 L of water per day, and breathes 20 m^3 of air per day. Factors for other test species are available (see Table VIII-2).

(5) Exposure to mixtures: The default assumption is that for chemicals causing the same effect, the doses are simply additive. For chemicals having different effects, assess the effect of each at its estimated exposure. If, however, the chemicals are known to interact (e.g., synergistically), then the estimated effect should be adjusted to reflect this information. Alternatively, if one (or a few) of the chemicals is sufficiently toxic and in such high concentration that it dominates the health effects, then the effects of the less potent chemical may be de minimis and can be ignored.

(6) Sensitivity differences: The default position is that explicit allowance is not made for sensitivity differences between individuals in the reference group and the exposed population. If the available data are for a general population or a population of low susceptibility for the given effect (e.g., healthy workers for respiratory dysfunction), then the risk estimate must be increased by some factor appropriate to the data. If the subject population is known to contain a significant percentage of subpopulations of especially suspectible individuals, then this fact should be used in the risk assessment. These factors should be derived after detailed consideration of any special subpopulations. For example, in 1983 children constituted 28.1% of the population and the birthrate was 15.9 live births per 1,000 total population per year.

(7) Combining response data: In some cases the response data reported in original publications can be combined to improve the reliability of the human risk estimations. The data, for example, may show tumors at more than one site in the animals tested, multiple teratogenic effects, or different neurotoxic symptoms in different persons exposed. Since the ultimate objective is to estimate the number of persons affected by environmental exposures, rather than the subcategories of effect, the varieties of an effect are combined. The data are summed assuming independence, but using the following equation to eliminate errors of multiple counting of the same individuals:

$$P[\bigcup_{i=1}^{m} A_i] = \sum_{i=1}^{m} P(A_i) - \sum\sum_{i<j} P(A_i)P(A_j) + \sum\sum\sum_{i<j<k} P(A_i)P(A_j)P(A_k)$$

$$- \sum\sum\sum\sum_{i<j<k<\ell} P(A_i)P(A_j)P(A_k)P(A_\ell)\ldots$$

where: P(A) designates the probability of effect A;

i, j, k, and ℓ are subscripts for the various effects; and

m is the total number of effects being combined. Note the alternating signs of the terms.

If differing estimates are available from multiple studies and none can be rejected on the basis of quality, probabilities are calculated from each data set and then averaged.* If the various effects are from different pools of animals as in teratology studies, the sample size will vary and the results are not readily combined. These results are therefore calculated separately and the probabilities of an adverse effect are then summed to give a total risk. This practice of combining data has been discussed as an approach in obtaining total estimates of carcinogenic risk in animals with one or more tumor sites (EPA, 1984). When both sexes of a species receive the same dose and express the same effects, data from the two sexes are combined for further calculations.

E. Health and Environmental Impacts Estimation and Integration

The results of the exposure prediction step are now combined with the health effects model to estimate the adverse effects on exposed individuals, and with information on exposed population groups to estimate the total number of cases of each kind of effect associated with each waste management alternative. The procedures are discussed in this section for exposed individuals and populations. Analogous procedures could, in theory, be applied to estimate ecological or other environmental effects, but are, in practice, much more difficult to implement quantitatively, and are discussed only briefly in this section.

1. Effects per individual: The probability of an exposed individual incurring a given adverse health effect is calculated by multiplying the concentration, C, of the chemical in the exposure medium** (as determined in the exposure analysis) by the extra risk factor R(d) at an equivalent dose in that medium as determined from the dose response data. If necessary, the product is also multiplied by any adjustment functions needed to correct for differences in biological conditions, f(b), or in the time f(t) (or other measure of interval) between the reference conditions and the exposure conditions. The overall equation is:

$$\text{Probability of effect} = C \cdot R(d) \cdot f(b) \cdot f(t)$$

A similar calculation is made as necessary for each effect that the chemical might cause, and for each chemical or group of similarly- acting chemicals to which the individual is exposed. If exposure occurs by multiple routes and the data base indicates that summation of the total intake is appropriate, the sum (in appropriately converted units) is used for C. If exposures are intermittent or less than lifetime and lifetime risks are desired, appropriate adjustments are included in the time function.

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* In regulatory applications, the geometric mean (nth root of the product of n probabilities) of this combined estimator has been used rather than the arithmetic mean, as it leads to a higher risk estimate at a given dose and hence a lower regulatory standard.

** i.e., water, air, food, soil, materials, etc. The intake quantity may be a more convenient parameter for environmental dose than the concentration in some analyses; it is obtained from appropriate intake assumptions.

Calculations are made for representative individuals in each significant exposure group identified. Typical representatives would be an average exposed individual, the most exposed individual, and average or most exposed child. Additional calculations are made as necessary for individuals in especially sensitive subgroups (see below). The results of the risk calculations are tabulated and combined as appropriate and reported in a form useful for decision making. For some decisions, the risks per individual may be adequate input, while for others, the risks to populations described below will be required.

2. Effects on populations: Comparison of the total adverse health effects of hazardous waste management alternatives requires applying the health risk factors as determined in the preceding sections to information on exposed populations. The present methodology focuses on exposures to the chemicals of concern incurred primarily by the public and secondarily by workers. In either case, the analysis is simplest for a homogeneous population uniformly exposed to a fixed level of a single chemical that produces one health effect. The case becomes more complex as multiple subpopulations, multiple exposure conditions, multiple chemicals, or multiple health effects must be considered.

The analysis is further complicated by the likelihood that the population will not remain of constant size, composition or location for the duration of the potential exposure period. Temporal assumptions are required before proceeding with the analysis. The simple assumption is often made that the present population pattern will continue throughout the period being assessed. In comparative assessment of hazardous waste management alternatives, however, special care should be taken to determine if this is a reasonable assumption. For example, changing residential, industrial, recreational or transportation patterns in an area over several decades could substantially affect the risks of having a landfill, incinerator or storage facility nearby. Hence, explicit statement of future population assumptions must be made.

A statement of the population risk is sometimes derived from an estimated individual risk by simple scaling. For example, the probability is multiplied by 10^6 to indicate the risk per million exposed persons, or the probability is multiplied by the total exposed population to estimate the number of cases. A more systematic procedure takes into account the variations in exposure conditions and of susceptibilities for exposed individuals, as described below.

a General population: The number of cases of a given adverse health effect incurred by the exposed group of individuals is estimated by multipling three factors: the concentration (C) or its dose equivalent from the exposure analysis; a risk factor R(d) from the dose-response relationship; and the number of persons (N) in the projected exposure group. The total number of cases is then obtained by summing across the factors:

$$\text{No. of extra cases} = C_1 \cdot R(d)_1 \cdot N_1 + C_2 \cdot R(d)_2 \cdot N_2 + \ldots C_n \cdot R(d)_n \cdot N_n$$

$$\text{or} = \sum_{1}^{N} C_i \cdot R(d)_i \cdot N_i$$

For a nonthreshold effect such as cancer where low dose linearity is assumed, the calculation for a residential area can be simplified by using the slope, k, of the dose-response line at low dose and the population-weighted average concentration, $\bar{C}$. The risk equation for the average exposed resident becomes:

$$\text{Average probability of effect} = \bar{C} \cdot k$$

and that for the population, N, becomes:

$$\text{Number of extra cases} = k \sum_{1}^{N} \bar{C}\text{-}N$$

The potentially exposed populations can be determined by identifying relevant geographical boundaries and by using current detailed population profiles, supplemented if necessary by extrapolated data. Several sources may be used for development of the population densities and the identification of subpopulations exposed under different conditions (e.g., different routes, levels, peaks, and continuity).

Results of the risk calculations are tabulated and combined as appropriate to reflect equity issues (e.g., geographical distribution).

b. Special subpopulations: If the exposed population contains subgroups that differ greatly in characteristics, then these also are considered, because they may be more susceptible to adverse effects. Some subgroups may be more susceptible in general (e.g., because of age or special health conditions). Others may be more susceptible to specific kinds of toxicants (e.g., teratogens for females in early pregnancy; allergens for many people), more susceptible because of exposures to chemicals from other sources, or likely to have a much higher uptake at a given exposure (e.g., children exposed to contaminated soil). Extremely difficult to quantify are those who may be more susceptible because of dietary deficiencies or preferences, or who are deficient in production of enzymes or hormones that are important to biological repair mechanisms. A sample worksheet for surveying the potential health effects on a number of subpopulations is given in Chapter X.

Generally, the geographical location of fixed structures (e.g., hospitals, schools, nursing homes, recreational areas, and private wells) within the area is sufficient to identify many specific locations where the general population densities can be modified for the subpopulation. Health data, some of which is regionally and locally specific, are available through the National Center for Health Statistics, Center for Disease Control, and state and county health agencies. Statistical data are available for numbers of individuals in different age groups, for birth rates, etc.

Determination of the exposure of the special subpopulations may be considerably more imprecise than that of the generally exposed population. The response to exposure may also be difficult to predict. These factors result in a correspondingly greater level of uncertainty in the estimated health effects.

c. Occupationally exposed workers: The assessment of health effects in exposed workers is conceptually the same as for estimating individual and public health effects. However, the places and conditions of exposure are different, the number of workers to be considered are usually relatively small, and the workers are usually in better health than the general population or sensitive subpopulations. In addition, monitoring of both the worker's health and exposures is frequently performed and reduces uncertainty in the risk assessment.

Quantitative estimation of occupational health risks requires substantial effort to develop site- and work-station-specific scenarios to estimate the exposures incurred by many different kinds of workers engaged in the various activities involved in treatment, storage, disposal, or transportation of the hazardous wastes and in corrective actions or cleanup operations in case of accidents, spills, fires, or leakage. Specific assumptions are required regarding the kinds and efficiencies of protective clothing and equipment utilized by the various workers and other work practices. More qualitative estimates of occupational risks can be useful in many hazardous waste management decisions.

For each waste scenario, the treatment, storage, disposal, transportation, and corrective actions will have been evaluated to estimate the likely routes, relative levels and numbers of worker exposures. The total or relative occupation risks of the alternative disposal technologies are then estimated on either a quantitative or qualitative basis as desired. Subpopulations of exposed workers are analyzed separately if desired in a rigorous treatment. The estimated effects are integrated for all worker subpopulations.

3. Special considerations: If the chemical of concern under a given exposure condition produces multiple effects, all are considered; each effect calculated with the appropriate risk factors and subpopulations. Note, however, that one or two effects may predominate (e.g., cancer) so that the others are neglected in the analysis without affecting its validity significantly. If the chemical under different routes of exposure produces the same effect but different response rates, the estimated effects of each exposure are summed for each subpopulation. If the chemical under different levels of exposure has multiple effects, then each of these combinations is considered separately for each subpopulation. If multiple chemicals that cause different effects (as with mixed hazardous wastes) are present, the effect of each on each subpopulation is examined. The effects of similar chemicals may be substantially similar, however, which simplifies the analysis. Similarly, one

effect may be of greatest concern because of its nature or because of the level of exposure to the chemical causing it, and the analysis is simplified.

If the effects are similar in severity, calculate the effects at each exposure and sum them, but if they are greatly dissimilar, aggregate but report separately for subsequent comparison of decision options, i.e., one may need to consider the treatment and disposal options to some extent on an effect-by-effect basis.

If more than one chemical is involved but they do not interact, several assessment alternatives exist. If the chemicals, their effects and exposure conditions are sufficiently similar (e.g., chlorinated solvents), one can simply sum their calculated exposures to estimate an overall health effect. As above, one chemical or one effect may predominate and the calculation can be simplified accordingly. If these factors are not sufficiently similar, then the different major combinations must be considered separately. Accounting procedures here require careful attention. In addition, this analysis would be further complicated if any of the chemicals present do interact, i.e., produce synergistic or antagonistic effects. These must also be taken in account. Adjustment factors of several kinds could be justified.

4. Environmental impacts estimation: The disposal of hazardous waste can affect the environment in many ways in addition to human health risks. Thus, environmental effects should be considered in a comprehensive risk assessment. On the simplest level, the environmental consequences can be addressed by identifying their presence and developing a rating based on their potential to damage the environment. Quantification of impacts, however, can be much more difficult to perform. A rudimentary examination of environmental effects in conjunction with a health effects assessment can be accomplished by following an approach similar to that discussed for human health effects: (a) data gathering, (b) identification of routes and levels of exposure, and (c) assessment of effects on exposed populations.

Data gathered for the purpose of running environmental transport models generally will be adequate to examine environmental effects. Site characteristics such as topography, depth to groundwater, soil type, vegetative cover, and distance to the nearest body of water are examples of information that will have been compiled. Identification of routes of exposure will have been one of the most important steps in the environmental assessment.

Using the information at hand, ratings that reflect the degree of perceived hazard should be assigned to exposure routes. Ratings definitions can be fairly broad, but still provide an indication of the level of environmental risk posed by a disposal alternative for a particular waste. Ratings of low, moderately low, moderately high, and high are convenient. A low rating indicates that either no or de minimis effects to the environmental media are predicted. A moderately low rating indicates that adverse effects will probably be noticeable but not of major significance to either the immediate locale or the general environment. A moderately high rating indicates that readily apparent environmental effects are predicted that will have a significant impact on the immediate site or transcend other environmental segments. A high rating reflects significant environmental effects that would lead to permanent damage to the surrounding environment; a high rating implies that a major environmental reason exists not to dispose of a waste via this management scenario. These ratings allow comparison among alternative TSD approaches for a given waste, but should not be used to compare different waste streams.

F. Uncertainty Analysis

The several available approaches to uncertainty analysis are reviewed in Chapter X. They range from largely qualitative discussion and survey of expert judgment through various levels of sensitivity (parametric) and statistical analyses, and aggregation methods. The choice of approach depends on several considerations, including the quality and quantity of information and data available to be analyzed, the type and range of risks being considered, the time and resources available to perform the analysis, and the purpose the analysis must serve, to note but a few.

The number and range of variables involved in estimating the health and environmental risks and the costs associated with hazardous waste management alternatives, coupled with the limitations of data and time that usually exist in real world decisions, will generally preclude a truly rigorous systematic approach. The present method, therefore, focuses on uncertainties in human health impacts (which often parallel but are more highly valued than environmental impacts, and of greater magnitude than uncertainties in monetary costs), and strives to give useful results within the existing limitations.

The approach is based on a combination of methods and involves three steps.

- Step 1 consists of a identification and qualitative discussion of sources of uncertainty in the analysis of each scenario. Best judgment estimates are then made of reasonable ranges of possible values of individual factors and parameters.
- Step 2 consists of a sensitivity analysis of selected factors and variables to define further their potential impacts.
- Step 3 consists of an aggregation of uncertainties across a given scenario by using a form of the propagation (cascading) of errors method.

These steps are described further below.

1. Sources of uncertainty: This step of the uncertainty analysis involves a systematic survey of each scenario and of the several parts of the associated risk analysis. Each of the boxes in the overall health assessment process shown schematically in Figure III-1 requires consideration. All input data, calculations or models, and assumptions made that could significantly affect the final result should be identified.

The potential sources of uncertainty can be tabulated under five major topic areas or factors. These factors parallel the essential steps in the sequential process of estimating the overall risk (i.e., number of cases of adverse health effects) of the alternative hazardous waste management methods. These major uncertainty factors are:

1. Pollutant Release - Assumptions and variables in the source assessment relating to the quantity and rate of release of hazardous substances to the environment from a hazardous waste TSDF site.

2. Environmental Transport and Fate Analysis Methods - Assumptions and variables relating to the environmental media, rates, and directions of transport away from the site and model validity.

3. Exposure Prediction - Assumptions and variables relating to the points in space and time that the chemicals of concern may interact with receptor populations and the resultant exposure levels.

4. Health Effects Analyses Information and Methods - Information and data from the literature relating to the health effects of the chemicals of concern, and to methods and models for converting this information into predictive dose-response relationships.

5. Health Impact Estimation and Integration - Assumptions and variables in estimating impacts of exposure on the individual populations and especially sensitive subpopulations exposed, and in integrating the impacts across all exposure levels, populations and subpopulations to yield an estimate of the number of potential cases of each type of adverse health effect.

Within each of the factors, numerous subfactors or variables exist that vary among wastes, TSD technologies, and management scenarios. A checklist of such subfactors is shown in Table IV-4. Relevant sources of uncertainty are tabulated and evaluated.

The number of variables will usually be large and statistical data will be marginal. Although exceptions may be possible, this usually precludes a detailed estimation of the probability distribution curve for each variable. Estimates based on overall information and judgment are made, however, of the most likely range in which the value would fall, e.g., within an estimated standard deviation (σ) of the best point estimate for a value. (About 68.3% of the values would fall within $\pm 1\ \sigma$ of the mean.) The extreme values would likely occur within two to three standard deviations (95 to 99% of the values) from the best point estimate. These ranges are based on the assumption of a normal (Gaussian or bell-shaped) distribution of values, a condition that will probably not precisely exist for many variables in the present kind of analysis. For the general distribution case (with σ^2 less than infinity), the extreme value occurrences are given by Chebychev's inequality as follows: $\pm 3\ \sigma$ contains 88.9% of the values and $\pm 4\ \sigma$ contains 94%.

2. Sensitivity analysis of key variables: Sensitivity or parametric analyses are most useful when a calculation, model, or laboratory

TABLE IV-4

FACTORS AND SUBFACTORS TO CONSIDER IN ANALYSIS OF UNCERTAINTY IN HEALTH RISK ASSESSMENT FROM HAZARDOUS WASTE DISPOSAL

1 Pollutant Release	2 Environmental Transport and Fate	3 Exposure Prediction	4 Health Effects Literature Base	5 Health Impact Estimation and Integration
Waste Parameters	Transport Parameters	General Population Parameters	Literature Base	Demographics and Lifestyles
Quantity	Through Air	Locations and Distributions in Space and Time	Types of Effects	Subpopulation Identification
Properties	Monitoring Data	Monitoring Data	Data Quality	Numbers Exposed
Constituents	Models	Exposure Parameters	Dose-Response Data	Estimated Effects
Disposal Parameters	Through Ground	Route	Species	Average Exposed Individual
Technology	Monitoring Data	Frequency	Route	Most Exposed Individual
Site	Models	Duration	Frequency	Sensitive Subpopulations
Transportation	Runoff	Concentrations	Duration	Occupational Exposures
Accident Potential	Monitoring Data	Peak	Concentrations	Multiple Effects
Sabotage/Vandalism Potential	Models	Average	Threshold Effects	Multiple Exposures
Release Medium	Disappearance Parameters		Available Extrapolation Models	Integration of Total Effects for Population
Volume Leachate	Decomposition		Duration	
Air Dilution	Degradation		High-to-Low Dose	
Release Rates	Stabilization		Interspecies	
Monitoring Data	Accumulation Parameters		Model Selection/ Development	
Models	Bioaccumulationn			
Quantities Released	Biomagnification			
To Air	Physicochemical Processes			
To Ground				
To Surface Water				
Models				
Temporal Parameters				
To First Release				
To Depletion				
Models				

experimental system contains a relatively small number of variable components with clearly defined (or observable) interrelationships. In nonexperimental systems, sensitivity analysis can address only those variables within a model or mathematical equation. In real decision making situations, however, the major uncertainties may lie in factors that an analysis finds impossible to fit into a quantitative model. As noted previously, the number of variables in the present comparative risk assessment of waste treatment, storage, and disposal scenarios is so large and the interrelationships so imprecisely known in some cases that a rigorous sensitivity analysis of all variables is precluded.

An analysis can be made, however, of the sensitivity of the final result to changes in key variables identified in the preceding step, and may be quite valuable in the determination of overall uncertainty.* This analysis can determine the critical ranges of these key factors. It may be particularly helpful in estimating the extreme value of a given variable that would have to occur before the overall risk of a disposal technology rose to some predetermined level of concern. An analysis of the impact of the simultaneous variation of multiple variables is precluded on a routine basis when the number of variables is more than a dozen as in the analysis of most examples of hazardous waste management.

Sources of uncertainty to be selected for sensitivity analysis vary by waste stream, scenario, exposure route, type of effect, and population characteristics. The general checklist of possible sources (Table IV-1) and the analysis of the preceding step will be useful in identifying key variables and assumptions for analysis.

3. Aggregation of uncertainties: The aggregation of uncertainty across a complete risk assessment for a given scenario is based on the propagation (or cascading) of errors methods. Quantitative measures of the uncertainty of many variables are not indisputably apparent, of course, so the method uses qualitative discussions, expert judgments by project staff members, and the results of the sensitivity analyses to estimate such values.

The overall risk calculation is structured, as shown in Chapter X, as a product of a series of factors, each representing an essential step in a series of steps. The equation is:

$$R = F_1 \times F_2 \times \ldots F_n$$

The upper and lower limits of the range of the risk (i.e., the uncertainty) may, with appropriate assumptions, be expressed exponentially as follows:

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* This statement assumes the key variables have been accurately identified. If they have not, the sensitivity analysis may given an inaccurate indication of the true state of uncertainty regarding the decision.

$$\text{Risk range} = \begin{cases} R \cdot 10^{|t|\,(U_1^2 + U_2^2 + \ldots\, U_n)^{1/2}} & \text{for } t > 0 \\ R \div 10^{|t|\,(U_1^2 + U_2^2 + \ldots\, U_n)^{1/2}} & \text{for } t < 0 \end{cases}$$

where R is the risk as calculated by "best estimate" values for all variables, the U_i^2 terms are the variances* of the logarithms of the individual factors, and $|t|$ is the absolute value of a decision parameter t that reflects the degree of confidence desired in the data.**

Although $|t|$ varies somewhat with the distribution (i.e., normal or various nonnormal distributions), decisions involving the comparisons of alternatives are relatively insensitive to the value of $|t|$ assigned. That is, if one is comparing the risks of four alternative hazardous waste disposal technologies for a given waste, one would want to use the same value of $|t|$ in the analysis of each, but the comparison can then be made about as well with all uncertainty ranges reflecting 68% confidence limits ($t = \pm 1$) as with all reflecting 95% limits ($t = \pm 2$), or 99% limits ($t = \pm 3$).

For a first approximation, therefore, t is assumed to be unity ($t = 1, -1$). The relationship above becomes:

$$\text{Risk range} = \begin{cases} R \cdot 10^{(U_1^2 + U_2^2 + \ldots\, U_n^2)^{1/2}} \\ R \div 10^{(U_1^2 + U_2^2 + \ldots\, U_n^2)^{1/2}} \end{cases}$$

or the aggregation of uncertainty is shown simply by the expression

$$10^{(U_1^2 + U_2^2 + \ldots\, U_n^2)^{1/2}}$$

If one considers the five major factors listed in Table VI-4 that cause uncertainty in the estimated number of cases of adverse health effects, then:

$$\text{Range of cases} = \begin{cases} \text{Best estimate of cases} \times 10 \sqrt{U_1^2 + U_2^2 + U_3^2 + U_4^2 + U_5^2} \\ \text{Best estimate of cases} \div 10 \sqrt{U_1^2 + U_2^2 + U_3^2 + U_4^2 + U_5^2} \end{cases}$$

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* Square of the standard deviations (or mean square error as appropriate).

** Note that if the best estimate of F_i for one variable is zero, the best estimate of the risk, R, is also zero and this method cannot be used in its simple form to estimate the range. While the best estimate of F_i is zero, the upper confidence limit on it is unlikely to be zero, and and this information can be used to estimate the upper limit on the risk.

A convenient format for summarizing the aggregation of uncertainties at this factor level is shown in Table IV-5.

TABLE IV-5

SUMMARY OF APPROACH TO AGGREGATION OF UNCERTAINTIES AT THE FACTOR LEVEL

	Uncertainty by Factor					
Waste Management Scenario	Release Factor 10^{U_1}	Environmental Transport Factor 10^{U_2}	Exposure Prediction Factor 10^{U_3}	Health Effects Data Base Factor 10^{U_4}	Health Impact Estimation Factor 10^{U_5}	Total Uncertainty Factor $10^{(U_1^2+U_2^2+U_3^2+U_4^2+U_5^2)^{1/2}}$
1						
2						
3	---------- (Each stated as estimated order or magnitude 10^U) ----------					
4						
5						

The uncertainties of the variables within a factor (Table IV-4) may be similarly compiled if they are multiplicative variables or they may be appropriately summed for those that are additive, or a combination of operations can be used as appropriate. A sample worksheet for tabulating these factors and parameters across waste management scenarios is illustrated in Table IV-6, in which space is provided for entry of names of up to five variables. The list of variables in Table IV-4 is a useful checklist, but could be expanded in different ways for different applications, and could probably be expanded significantly for a specific application.

Four difficulties in performing such an analysis are readily identified. First, the number of individual sources of uncertainty (the subfactors or variables noted in Table IV-4) that can be identified in a comprehensive analysis may be so large (perhaps a dozen or more) that considerable effort will be required to acquire available data and estimate the probability distribution of each. Secondly, the inadequacy of the available data* may force considerably more dependence on expert judgment than preferred in estimating uncertainties. Thirdly, the interrelationships between the subfactors may be diverse--some may combine multiplicatively, some arithmetically; some may be independent, but others may not--and the degree of interdependence may not be readily ascertained;--and some may be dominant or key variables. A detailed mathematical model would be needed. Finally, the uncertainty about the best point estimate for a given variable may be quite unsymmetrical; i.e.,

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* A larger data set is required for estimating bounds than for a point value.

TABLE IV-6

WORKSHEET FOR PROPAGATION OF ERRORS IN ANALYSIS OF UNCERTAINTIES IN HEALTH RISK ASSESSMENT OF HAZARDOUS WASTE MANAGEMENT ALTERNATIVES

WASTE MANAGEMENT SCENARIO		RELEASE FACTORS						TRANSPORT FACTORS						EXPOSURE FACTORS						DOSE-RESPONSE FACTORS						HEALTH EFFECTS INTEGRATION						TOTAL UNCERTAINTY
		Variables					Total, Factor	Variables					Total, Factor	Variables					Total, Factor	Variables					Total, Factor	Variables					Total, Factor	
No.	Short Title	v_1	v_2	v_3	v_4	v_5		v_1	v_3	v_3	v_4	v_5		v_1	v_2	v_3	v_4	v_5		v_1	v_2	v_3	v_4	v_5		v_1	v_2	v_3	v_4	v_5		
1																																
2																																
3																																
4																																
5																																
6																																

Source: MRI

the probability distribution may be quite skewed. An average uncertainty range is therefore less preferred for every variable than an explicit statement of the upper and the lower ranges for it.* Separate aggregation would be desirable for upper bounds and lower bounds. (Care would be required so that the upper bound on each variable was defined consistently to correlate with an upper bound on the estimate of health effects.) The net result of these difficulties is that a comprehensive quantitative analysis of uncertainties can require a substantial investment of time and resources to acquire data and perform the analysis.** Some compromise is inevitable in analyses having limited time and resources available, but the compromises in the present approach would be made on a scenario-specific basis.

The calculated uncertainty of the overall health risk estimate seems paradoxically to always increase with the number of factors and variables one includes (the level of detail of the analysis), although the total amount of information on which to base a decision should have been usefully increased by including these details. One must consider two sources of error to resolve this apparent paradox: variant and bias.

One is estimating risk by incorporating a number of factors into a model. The model is by necessity an approximation. Thus, to the extent that the model is incomplete, there will be a systematic or bias error introduced. Each term of the model must be estimated from data. The estimates will have some variance associated with them. The more terms estimated in the model, the larger the variance of the estimated risk. However, the more terms included, the better the model should approximate reality. Thus, as one increases the number of factors or variables, the uncertainty due to sampling consideration (variance) will increase, but the uncertainty due to incomplete model will decrease.

The total uncertainty is the sum of these two terms. One increases as the number of factors increase, the other decreases. In order to reduce variability of the estimate, more data about each factor or variable (larger sample size) is needed. Uncertainty analysis identifies the major component leading to uncertainty and so identifies areas where studies may reduce the uncertainty the most.

In summary, the propagation or cascading of errors approach to aggregation of uncertainty can be used in a less than completely rigorous manner to give an approximation of the total uncertainty. A review of the operable variables and a general knowledge of the realistic ranges of the pertinent parameters in the specific scenario can be used to estimate the total uncertainty for each factor. These estimates are then explicitly stated. While different authorities will undoubtedly have different judgments on the magnitude of some of these uncertainties, their explicit statement as in the present approach would provide a platform for further testing, discussion, and improvement.

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* A reviewer has noted that for many decisions, a best estimate may be the more useful parameter, but that a sensitivity analysis of more extreme values in the range can be used to supplement the best estimate.

** A computer model could be developed and tested if such analyses were to be performed on a routine basis.

V. SOURCE ASSESSMENT (HAZARD CHARACTERIZATION)

The source assessment portion of a risk assessment contains two major components: (a) hazard identification and description; and (b) quantification of releases of environmental contaminants. Source assessments can be performed at various levels of detail, ranging from simple to complex. They can be global or site specific, consider existing or proposed facilities, and take a single medium or multimedia approach. Definitive source assessments require substantial inputs of information and data, but model sources, scenario approaches, and engineering estimates can help yield useful results when the data base is limited.

A. Hazard Identification and Description

In Chapter II, hazards were described as potential sources of adverse effects. Where chemical technologies are involved, specific materials, conditions, and activities all might be deemed hazardous. Hazardous materials are those having intrinsic physical or biochemical properties that pose risks to human health or the environment when the materials are present in sufficient quantities and are not properly controlled. Hazardous wastes, the focus of this study, meet this criteria by regulatory definition (EPA, 1981). Hazardous conditions or activities are those having significant potential for allowing hazardous materials to escape from a controlled to an uncontrolled state in quantities sufficient to pose risks; that is, the conditions hold potential for significant release of pollutants to the environment from a site or process.

Assessments of the chemical(s) of concern and their source(s) are often done concurrently. A good starting point is frequently the examination of known or potential sources of environmental contaminants.

1. Technoeconomic characterization: This step involves compilation and evaluation of information on technical, geographic, and socioeconomic aspects of the potential sources of environmental contamination.

Potential sources of hazardous waste are too many and varied to list individually, but those likely to cause environmental contamination can be placed in three major categories:

- Production and Distribution Processes--e.g., manufacturing, formulation, transportation accidents
- Product Use Patterns--e.g., unused agricultural chemicals, spent solvents or treatment liquors, recalled products, accidentally contaminated products,
- Hazardous Waste Treatment Storage and Disposal Facilities (TSDFs), e.g., storage tanks, waste piles, incinerators, landfills (active or closed), chemical reaction, or adsorption processes.

Sources may be described as being a specific facility or site, or they may be aggregated on some basis, e.g., by industry or region. Hushon and Clerman (1981) have emphasized the need to take a life cycle view in assessing the hazards of a chemical including its disposal at several points.

Information on production, distribution and use patterns varies substantially in availability among chemicals: excellent reviews or trade literature sources may be available for some; EPA industry studies, business information supplied to EPA, or personal contacts may be the best source for others, and substantial data gaps (particularly from a site-specific view) may exist for many. Two frequently useful sources are Kirk-Othmer (1979) and SRI (1984). In cases where data are inadequate, useful estimates can result from analysis of information on processes, production capacity, markets, and similar sources. For many exposure assessments and comparative risk assessments, reasonable hypothetical scenarios can be constructed and tested to give useful information. Guidelines for scenario construction for comparative risk-cost-benefit assessment are given in Appendix B.

2. Chemicals of concern and their properties: In some assessments, the chemicals may be predetermined by the EPA, based on a regulatory agenda or on petitions from parties-at-interest. In other cases, a preliminary evaluation of a complex mixture of chemicals may be necessary to select those to be assessed in detail. A comprehensive assessment should identify all chemicals that reasonably could be expected to pose significant risks. The assessment includes evaluation of concentrations, amounts present, and possibility of release to the environment, and a preliminary evaluation of their physical, chemical, health effects and environmental properties. Handbooks, such as that by Verschueren (1983), and environmental chemistry reference works (e.g., Stumm and Morgan, 1981) are useful sources. When data are unavailable, information on related chemicals sometimes can be used with extrapolations, analogies, or structure-activity relationships for reasonable approximations. Lyman et al. (1982) provide one useful resource for chemical property estimation. The evaluation should identify those chemicals most likely to be released from the source and cause adverse effects.

Health effects to be considered include: general toxicity; oncogenicity (causes tumors) and carcinogenicity (causes cancer or leukemia); mutagenicity (causes mutations); teratogenicity (causes deformed fetuses); sterility or decreased reproductive success; behavioral effects; and cellular or subcellular effects. Useful information and data sources include literature reports on controlled toxicological studies, clinical observations or epidemiological studies on humans; acute, subchronic, chronic and special toxicological testing with laboratory or domestic animals; toxicological tests with microorganisms; and pertinent biochemical tests.

3. Release mechanisms and points: This step involves engineering analysis of production, distribution, use or disposal processes as necessary to determine specific process activities and points at which the chemicals of concern are released or escape to the environment. Both the route of release and the receiving environmental media should be identified for each chemical of concern.

Chemicals can be released into the environment by several routes: manufacturing emissions to air as vapors or particulates and discharges to water in solution or suspension; dissipative uses, such as pesticide application; insecure disposal of unused materials and wastes, followed by runoff, leaching or volatilization; and accidents, such as tank truck spills, warehouse fires, etc. Careful attention must be given to potential accidents and emergency arrangements as well as to conventional operations. Safety audits, hazard indices, hazard surveys and operability analysis are terms used to describe some systematic approaches to such studies.

Chemicals may be released from the source into air, water, or land. For purposes of environmental transport modeling, receiving compartments are conveniently viewed as: local, regional, or global, for emissions to the atmosphere; watersheds, streams and rivers, freshwater impoundments, estuaries, and seas or oceans for effluents; unsaturated zone and aquifers or saturated zone for leaching to groundwater; and surface, subsurface soils, and deep strata for disposal on land.

B. Quantification of Releases

Quantification can involve either estimating releases of chemicals from the source under existing conditions or under one or more sets of assumed future conditions. In either case, historical data on quantities released from the industry, process or specific release points usually are evaluated for guidance (Conway et al., 1982). Data on quantities and rates of release are available from sampling and analysis studies for many industrial operations, and ambient monitoring data near others may be useful in inferring releases. Average air emission factors have been developed for many processes (EPA, 1983).

Detailed scenarios are often useful devices for structuring estimates or predictions by appropriate analytical techniques, such as event tree and fault tree analysis, trend extrapolation and mathematical modeling. The development of scenarios usually requires preliminary characterization of the site(s) of the source(s) (e.g., hydrogeological and meteorological parameters), since the quantity of chemical release can vary with the site.

Mathematical models can be valuable in the prediction of the time and magnitude of potential releases. Predictive models typically require physical property data on the chemicals of concern, such as: melting and boiling points; vapor pressure or volatilization rates under various conditions; solubility in water, in organic solvents and in the presence of complexing agents; and vapor or liquid density. For a given chemical, the nature of the medium it is in within the source may greatly affect its release rate, e.g., an otherwise mobile chemical may have very low mobility if it is adsorbed on clay or distributed within a water-insoluble tar.

Recommendations, guidelines, and standards have been published for hazardous waste TSDFs (e.g., TRW, 1973; Chapman, 1982; EPA, 1983a, 1983c). Rates and quantities of materials released from hazardous waste TSDFs have been studied less to date, however, than those from many sources in the manufacturing and use categories. Since they are of primary concern to this project, however, they require further comment here.

- Releases during treatment: The potential for releases during treatment of a hazardous waste depends on the technique being used (e.g., stabilization, neutralization, reduction/oxidation, solidification, and extraction). Frequently, treatment methods are analyzed on a waste-stream-by-waste-stream basis; as a result, the applicability of the method to a particular waste must be determined before the waste release potential can be assessed for a method. The potential release could come in the form of fugitive emissions, process emissions, a spill, or an accident in which a large quantity is released. The form of the release also will be waste specific since the waste's chemical and physical characteristics will influence the type and quantity of release. The availability of data to quantify the amount and probability of waste releases during treatment will be dependent on the particular waste and the treatment techniques being studied.

- Releases during handling: In the process of handling wastes, several points can exist at which pollutants are regularly or irregularly released to the environment. Major potential release points are first identified and then amounts released must be quantified. As with treatment, handling releases are dependent on the specific properties of the waste and on the characteristics of the system. Because data for the release of a particular waste are not always available, it is often necessary to use release data for similar wastes subjected to similar handling practices. In some cases, consideration of appropriate environmental transport parameters may be useful in estimating release rates.

- Releases during transport: Releases during the transport of hazardous wastes may occur as a result of improper containment or accidents. The analysis involves estimating the probabilities of occurrence of releases (particularly from accidents) at different locations and the amounts of material likely to be released. Data of this sort have been compiled in a report that assesses releases and costs associated with truck transport of hazardous wastes (Abkowitz et al., 1984a). A similar report has been completed on rail and waterborne transport of hazardous wastes (Abkowitz et al., 1984b). Data to compile these reports came primarily from the Hazardous Material Incident File (HAZMAT) maintained by the U.S. Department of Transportation, Materials Transportation Bureau.

- Releases during disposal: Waste releases during disposal operations can be a significant route of exposure to human populations. The releases can be the result of failure of one or more components of the system (e.g., liner failure or failure of a leachate collection system for a landfill) or a process emission (e.g., stack emission from an incinerator).

In some cases, mathematical or computer models can be used to predict releases at a TSDF. Fugitive air emissions from landfills, for example, can be predicted using an equation based on soil bulk density, vapor flux of the chemical from the soil, soil porosity, and vapor density of the chemical (Farmer et al., 1980). Farino et al. have evaluated models for estimating air emissions from hazardous waste TSDFs. EPA (1985) has assessed emission problems during incineration of hazardous liquid organic wastes. Ehrenfeld and Ong (1984) have evaluated emission controls for hazardous waste TSDFs.

Predicting releases to groundwater from land disposal facilities is more complex because there are many components of the system that can fail. For example, interactions between leachate and clay barriers can be complex (Anderson and Jones, 1983; Daniel, 1984). One approach is to assume that if the containment and leachate collection systems have failed, then contaminant concentrations in the leachate released will be approximately the same as that given in a simple leaching test on a sample of the waste (using leaching conditions assumed to simulate those in the land disposal facility). Mathematical modeling approaches are of recent interest also.

A model under development that attempts to make quantitative predictions is the Pope-Reid Associates Land Disposal Failure Model (PRA, 1984; 1985). The model provides estimates of leachate releases from hypothetical land disposal facilities (landfills, surface impoundments, waste piles, and land treatment units) having a variety of design configurations. The facilities can reflect several different climatic regimes. The model can be run to give annual outputs, if desired, with benchmark times (time periods over which the hypothetical facilities have aged) of up to 200 years. The model computes the proportion of facilities in the hypothetical population that have failed and the expected volume of leachate released from such facilities.

Air and water monitoring data in the vicinity of representative sources can at times provide a useful basis for making estimates when site-specific data are limited. Care must be taken, however, that the monitoring data are not confounded by multiple contamination sources, problems well known for air and surface water and more recently recognized also for groundwaters (OTA, 1984).

- Catastrophic releases scenarios: Catastrophic releases of hazardous substances during storage, processing, or transport of large quantities of wastes are low probability, but potentially high consequence events. They would pose serious occasions of intense occupational and public exposure to health and safety risks and of substantial local ecological damage. Such releases could be initiated by either natural events, such as floods, tornadoes, lightning, and earthquakes, or human activities such as spills, fires, transportation accidents on land or sea, and acts of vandalism or terrorism. Issues, methods, and case studies involving low probability but high consequence risks were described in over 40 papers at a recent meeting (Waller and Covello, 1984). The methodology for assessing such risks is less developed than that for more typical risks, and further development of it is beyond the scope of the present study. In general, scenario approaches are required, but the outcome is quite dependent on assumptions about technologies, sites, timing, operation of failure prevention/detection measures, and human behavior. In particular, results can depend on what assumptions are made concerning contingency accident management plans and consequence mitigation measures that are at hand.

For hazardous waste disposal, the releases, exposures, and impacts will depend on the nature of the waste in a given assessment, on the site of catastrophic release, and on assumptions concerning the timing and efficiency of protective and corrective actions. In some cases, the nature of the waste and the disposal technologies might make negligible the probability of catastrophic releases from many or even most causes. For example, a nonflammable sludge of low volatility, low solubility in water, and high viscosity could be cleaned up with minimum risk in event of a large spill from an overturned truck. In view of the usual time and resource limitations, efforts to assess such risks could be reasonably minimized in the health and cost assessment.

On the other hand, attention may be required for the risks of flooding during cleanup of an old hazardous waste disposal site or for the risks of loading/unloading activities in transporting wastes for at-sea incineration. At a minimum, transportation risks should be discussed qualitatively; subsequent quantitative analysis may be desirable before ultimate decisions are reached. The qualitative analysis should note the worst reasonable case scenario, e.g., a maximum release at the most populous or most difficult to clean-up point in the route. In general, the more decentralized the hazardous wastes, the lower the risks of catastrophic release, the more centralized the waste disposal technology, the greater the potential for catastrophe.

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VI. PREDICTION OF ENVIRONMENTAL TRANSPORT AND FATE

A critical part of most chemical exposure assessments is the prediction of the movement and reactions of the chemicals between their sources (points of release) and the points in space and time at which they might reach human or other receptors (Neely and Blau, 1985). Comprehensive assessments must consider all major pathways of transport and any transformation of the toxic material between the points of entering the environment and points of exposure (Blau, 1985). Pathways include atmospheric and aquatic transport (resulting in inhalation or ingestion in drinking water or through the skin) and passage through the terrestial and aquatic food chains into human foods. Transformations may include chemical and biological reactions and intermedia transfers. Multimedia exposure assessment can become the most resource-demanding part of an overall risk assessment of a hazardous material, but partial exposure assessments can often provide information useful for many regulatory deliberations.

Several hundred environmental transport models have been described. Their classification is not easy. Broad categories include water models, air models, ecological models and intermedia models. Water models are generally divided into surface water and groundwater models, and the latter into those that address the unsaturated or variably saturated (vadose) zone and the saturated zone or aquifer. Increasingly, however, newer models can address both the unsaturated and saturated zones, or the interactions between surface water and groundwaters, or other multimedia interactions. Media models are also commonly classified according to their mathematical basis or type of application. This chapter discusses the kinds of data generally required for analysis of environmental transport and fate and the mathematical models that are available for specific pathways.

A. General Data Requirements and Sources

Information on the physicochemical properties of the specific material are important in evaluating transport and fate in the environment. These properties include: melting and boiling points; volatility; solubility; viscosity; photolysis rates; hydrolysis rates; oxidation/reduction rates; atmospheric reaction rates with ozone or hydroxyl radical; biotransformation rates; vapor particle size and density; octanol/water partition coefficient; soil adsorption coefficient; and other sorbtive properties. Some of these properties are specific to transport in aqueous environments and others to transport in air environments. Each property plays a significant role in predicting the transport and fate of specific chemicals. Methods are available to assist in estimation of chemical properties (Lyman et al., 1982; Paterson, 1985). Callahan et al. (1979) review the water-related environmental fate of 129 priority pollutants. Hushon and Clerman (1981) have reviewed information sources for the overall exposure assessment process. Donigian (1981) discussed field validation and error analysis in modeling the fate of chemicals in the aquatic environment.

- Site characteristics: Information and data are needed for both the major physical parameters of the site and the locations of populations of concern. Physical characteristics of the site and the surrounding terrain are important factors in selecting the most applicable transport models. The types of information about the site and surrounding locale which are of interest include:

  - Specific geographic location
  - Topographic maps
  - Soil maps
  - Nearest body of water
  - Drainage pattern
  - Types of emission sources
  - Stack height and plume rise factor (if applicable)

The exposed population, which includes workers at the site as well as the people living in the vicinity, is discussed further in Chapter VII.

- Physicochemical parameters: Soils data required for a variety of transport and fate models--including many surface water and groundwater models--can be obtained from a number of sources. The best source is county soil survey reports published by the U.S. Department of Agriculture, Soil Conservation Service. General soil maps are also available from the state Soil Conservation Service office. Soil scientists knowledgeable of particular soil properties can also be found in this office and in the agriculture department of the state land grant university. Examples of information needed for some models are: soil type, organic matter content, pH, bulk density, moisture content, particle size distribution, temperature, vegetative cover, slope and slope length, soil erodibility, and soil management practices.

Surface water data are necessary for storm water runoff and stream models. One of the largest data bases with this information is STORET (Storage and Retrieval for Water Quality Data) maintained by EPA. Other useful data, such as storm hydrographs and high/low stream flows, can often be obtained from agencies such as the U.S. Geological Survey (USGS), U.S. Army Corps of Engineers, Federal Insurance Administration, and state environmental and water resource agencies. Examples of data and information that might be required in some models are:

- Stream flow rates, pH, temperature, and dissolved oxygen
- Stream sediment load
- Background water quality
- Storm hydrographs for individual sites
- Surrounding land uses

Groundwater transport models are necessary to predict movement of a hazardous pollutant through the soil unsaturated and saturated zones and to predict distribution of the contaminant in the groundwater aquifer. Data to run these models can often be obtained from sources such as the USGS, state water resource boards, groundwater management districts, state and municipal health departments, and municipal water supply departments. Although it appears that there are many sources of information, obtaining hydrogeologic data for specific model parameters can be difficult because there are so many hydrogeologic parameters to quantify. Best estimates must frequently be made. Examples of typical groundwater parameters needed by groundwater transport models are:

- Hydraulic conductivity
- Hydraulic gradient
- Transmissivity
- Actual aquifer porosity
- Effective porosity
- Depth to groundwater
- Saturated thickness
- Transverse and longitudinal dispersivities
- Seepage velocity
- Bulk density
- Recharge rate
- Soil permeability

The use of air transport models for multimedia exposure assessment requires certain information, including meteorological data, physical and chemical properties data for the substances, and source emissions inventories. Meteorological ambient air data can be obtained from sources such as the Stability Array (STAR) data base of the National Oceanic and Atmospheric Administration and Storage and Retrieval of Aerometric Data (SAROAD) of the EPA. Typical meteorological data required for most air models include:

- Wind speed
- Prevailing wind direction
- Precipitation
- Atmospheric stability
- Cloud cover
- Maximum and minimum daily air temperatures
- Mixing height
- Solar radiation flux

Other selected meteorological data may be required for specific air transport and dispersion models.

- Biological parameters: Assessment of environmental transport and fate processes is greatly complicated if the pollutants interact with living organisms in the environment. Data requirements increase substantially, but the available data base is often fragmentary. The nature and extent of the biotic interactions will vary significantly with the physical, chemical, and biochemical properties of the specific substances of interest and with the populations of organisms at the specific sites being analyzed. These interactions occur primarily in the terrestrial and aquatic systems, although interactions in atmospheric and groundwater systems are not precluded.

The kinds of data needed include:

- Uptake through different processes (e.g., ingestion in diet ingredients; absorption from water or soil). Uptake rates can differ greatly among species and classes of chemicals. The data base is in a relatively early stage of development.
- Metabolic reactions that activate, convert, degrade, or decompose the chemical; processes that lead to excretion of it or its metabolites; and toxic effects that might kill the organism. Pollutants in the environment are generally metabolized to the greatest extent by microorganisms in soil and water, but metabolism can also occur to a substantial extent in many plants and to a lesser extent in fish, birds, and higher animals. A substantial literature exists on metabolism of chemicals, but data are very uneven among different species and classes of chemicals. Structure-activity correlations have been made for many combinations.
- Bioaccumulation or bioconcentration is the uptake of a chemical from the surrounding medium by an organism and retention of it at a higher concentration than in the medium. This process occurs for many aquatic and soil organisms. It occurs readily when the chemical is much more soluble in fatty and lipid tissues than in water (e.g., chlorinated hydrocarbons) or when it binds tightly to components of the organisms (e.g., certain heavy metals with proteins or bone). Sufficient research has been performed on bioconcentration that useful generalizations are available to make reasonably good estimates, even if the data base is incomplete on a specific chemical.
- Biomagnification involves the successive increase in concentration of a chemical along the components of a food chain (e.g., plants, insects, fish, birds of prey). Organisms at the top of the food chain such as predators and raptors are at the greatest risk. Analytical data are available on levels of chemicals in many food chain species in the field. Model ecosystems have also been used to study many chemicals and classes of chemicals. The data base and theoretical development are sufficient that reasonably good estimates of biomagnification can be made for many pollutants in given environmental settings.

- Interbiotic/intermedia transfer refers to the role of organisms in mobilizing pollutants or their metabolites from one environmental medium to another, e.g., metabolism of hazardous waste components by microorganisms may lead to solubilization, volatilization, or plant uptake of toxic chemicals; bioaccumulation of soluble toxics by aquatic organisms may be followed by transfer to bottom sediments or to terrestrial species. Such processes generally are not believed to be as important in exposure assessment as other processes cited, but the data base is relatively sparse.

B. Groundwater Models

Contamination of groundwater is a major concern with many methods of hazardous waste management. Intense efforts have been made recently to understand groundwater transport and to develop methods for predicting the rates and quantities of contaminants moving from point of entry to points of human exposure. Recent reviews of groundwater models include those of Bachmat et al. (1980), Jenne (1981), Oster (1981), Javandel et al. (1984), BPNL (1984), and Fenstermacher and Ottinetti (1987).

The primary mechanism that governs transport of pollutants in groundwaters is convection of dissolved chemicals as water moves through the soil matrix. Solute transport is retarded by adsorption-desorption interactions between the solute and the soil matrix. These interactions are commonly quantified using the soil/water distribution coefficient, K_d. Chemical characteristics and field conditions which increase the potential for groundwater contamination include: (1) the chemical has water solubility greater than 30 ppm; (2) the chemical is negatively charged at ambient pH; (3) the coefficient K_{oc} (defined as K_d divided by soil organic carbon content) is less than 300 to 500; (4) the chemical's degradation half-life is greater than 2 to 3 weeks; and (5) total precipitation is greater than 10 in/year (Travis, 1985).

Dozens of models are now available for predicting or comparing the movement of groundwater contaminants under various conditions. They include mathematical models that are fairly demanding of input data and ranking models that may be used in emergency response situations. Both types of models are reviewed in this section.

1. Mathematical models: Mathematical models can provide estimates of contaminant concentrations in groundwater at specific points of interest. These models may be subdivided into two groups, analytical models and numerical models, but other classifications are also used. For example, in practical analyses, one must consider whether the models focus on the unsaturated zone or the saturated zone, although some models can address both zones.

Mathematical models also can be categorized as random or deterministic. Random models may be either statistical and based on empirical data (i.e., using statistical methods to make predictions without attempting to simulate physical processes), or stochastic (i.e., using probabilistic predictions based on simulation of physical parameters). Deterministic models assume that the parameters in the cause-effect relationships and other uncontrollable variables are fixed or known, and then determine an optimum value for some variable of interest. The review below follows the analytical/numerical classification.

Both analytical and numerical models are based on partial differential equations describing groundwater flow and solute transport. Both types of models frequently use reference grids* superimposed on two or three dimensional maps of the aquifer in question, and both have similar kinds of input and output parameters. The distinction between analytical and numerical models lies in a fundamental difference in the mathematical approach. In analytical models a continuous function is evaluated as such to produce a straightforward single answer. In numerical models a continuous function is broken up into small discrete units and solutions are calculated for each unit and aggregated, making the use of a computer desirable (Keely, 1983). A good analytical model can be superior in some respects to numerical models since it avoids round-off and discretionary errors. The major drawback of analytical models is that they usually cannot be solved in functional form without extensive and often unrealistic simplification. The major drawback of numerical models is that error analysis is usually impossible except in the simplest cases.

This study identified about 30 models that could be considered for use in predicting solute transport from hazardous waste disposal sites. Table VI-1 lists 22 models that were evaluated; capsule descriptions of these are given in subsection (c). Table VI-2 lists other models that were considered.

Detailed information on data management within the context of specific analytical or numerical models is beyond the scope of this review. A few of the more valuable resources include Mercer and Faust (1981), the groundwater model data base at Holcomb Research Institute (1983), EPA (1982a), and BPNL (1984). Another valuable source of information is the EPA Robert S. Kerr Environmental Research Laboratory, Ada, Oklahoma. Analytical and numerical models are compared following potential applications, and limitations of each type are noted.

a. Analytical models: In analytical models, relationships usually are simplified by assuming steady-state conditions relative to fluid velocity, dispersion dynamics, and other physical parameters (Kufs et al., 1980). This simplification results in equations which can be solved in functional form to calculate specific values for parameters of interest, i.e., dilution, dispersion, and attenuation of groundwater contaminants. In cases where the broad assumptions are valid for the actual hydrogeological system being modeled, this approach yields rapid, efficient results. The usefulness

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* The use of analytical models does not require the use of grids, while the use of numerical models necessarily involves grids (Keely, 1983).

TABLE VI-1

GROUNDWATER SOLUTE TRANSPORT MODELS EVALUATED

Code Name	Applicable Zone	Model Type/ Characteristics	Reference
AT123D	Saturated	Analytical; 1-, 2- or 3-Dimensional	Yeh, 1981
BIOFILM	Vadose/Aquatic*	Microbial Degradations	Rittman et al., 1980
CFEST	Saturated	Numerical; 2- or 3-Dimensional	Gupta, et al., 1982
FEMWATER/FEMWASTE	Unsaturated/ Saturated	Numerical; Multi-Dimensional	Yeh and Ward, 1980, 1981
FIESTA	Saturated Geochem	Numerical; 1-Dimensional	Theis et al., 1982
McWhorter-Nelson	Unsaturated	Analytical; 1-Dimensional	McWhorter and Nelson, 1979
MINTEQ	Saturated	Numerical; Geochemical	Felmy et al., 1983
NRC-SLB	Unsaturated	Numerical; 1-Dimensional	Lester et al., 1981
PATHS	Saturated	Semianalytical; 2-Dimensional	Nelson and Schur, 1980
PESTAN	Surface*/ Unsaturated	Analytical; 2-Dimensional	Enfield et al., 1982
PLUME	Saturated	Analytical; 2-Dimensional	Wagner, 1982

TABLE VI-1 (Concluded)

Code Name	Applicable Zone	Model Type/ Characteristics	Reference
Plume Management	Saturated	Analytical; 2-Dimensional	Wilson and Miller, 1978
PRZM	Root Zone*/ Unsaturated	Numerical	Carsel et al., 1982
SESOIL	Surface/ Unsaturated	Semianalytical; Compartmental	Bonazountas and Wagner, 1981
SWIFT	Saturated	Numerical; 3-Dimensional	Dillon et al., 1978
SWIP2	Saturated	Numerical; 3-Dimensional	INTERA, 1979; USGS 1982
TRANS (Random Walk)	Saturated	Numerical; 1- or 2-Dimensional	Prickett et al., 1981
TRUST/MLTRAN	Unsaturated/ Saturated	Numerical; Multidimensional	Narasimhan and Witherspoon, 1977; Reisenauer et al., 1982
UNSAT1D	Root Zone/ Unsaturated	Numerical; 1-Dimensional	Bond et al., 1982
USGS-MOC	Saturated	Numerical; 1- or 2-Dimensional	Konikow and Bredehoeft, 1978
VHS	Unsaturated/ Saturated	Analytical; 2-Dimensional	Domenico and Palciauskas, 1982
VTT/MMT1D	Saturated	Numerical; 2-Dimensional	Kipp et al., 1976

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* Includes microbial degradation capability.

TABLE VI-2

ADDITIONAL GROUNDWATER SOLUTE TRANSPORT MODELS IDENTIFIED

ANALYTICAL MODELS	
Ground Mounding	Ortiz et al., 1979
Leachate Plume Migration Prediction	Kent, 1982
Screening Procedure	Falco et al., 1982
NUMERICAL MODELS	
Pollutant Movement Simulators	Khaleel and Redell, 1977
FE3DGW/MMT1D	Gupta et al., 1979
GEOCHEM	Sposito and Mattigod, 1980
Leachate Travel Time Model	EPA, 1982a
Solute Transport/Groundwater Flow	Porter, 1982
Leachate Organic Migration and Attenuation Model	Sykhes et al., 1982

of such solutions, however, is directly dependent on adequate verification of assumptions by field observations. Analytical models are generally inappropriate for aquifers with complex boundary conditions or other characteristics which do not permit the necessary assumptions.

Models which are designed for hazardous waste site evaluations for potential groundwater problems are frequently applicable to several scenarios. Because these models are designed for speed and ease of application, they have limitations. Of the models listed, the AT123D (the Analytical Transient one-, two-, or three-Dimensional model) appears best able to model waste transport in both saturated and unsaturated zones. It uses a simple analytical approach to estimate concentrations with minimal input data. SESOIL (the Seasonal Soil model) simulates water flow and chemical concentrations in the unsaturated zone. The McWhorter-Nelson model is a hydraulic expression useful for selected applications in the unsaturated zone that do not require consideration of adsorption interactions. None of the models addresses secondary porosity, immiscible liquids, or multiple contaminants.

Data requirements for the use of analytical models fall into three categories: aquifer boundary conditions, hydraulic variables, and contaminant concentration variables. Boundary conditions include head distributions, types of boundaries, flux points, and media thicknesses. Hydraulic variables include porosity, hydraulic conductivity, dispersion coefficients, and attenuation coefficients. Contaminant concentration variables include initial concentrations, release rates, and flushing rates (Kufs et al., 1980).

Input-output parameters for individual analytical models vary somewhat; Table VI-3 presents an illustrative input-output breakdown for the tandem PESTAN/PLUME model. No attempt is made to define fully the parameters in this example. The listing is presented as an illustration of the scope and complexity of the input and output parameters commonly associated with analytical models.

Analytical models are applicable to groundwater analysis where substantial data describing the physical system are available and where those data confirm aquifer homogeneity and the absence of complex boundary conditions. The margin of error for analytical model output is primarily due to the margin of error carried into the model by the uncertainty of input parameters; problems presented by inherent model weaknesses are minimal in comparison. Consequently, the margin of error accompanying mass transport outputs for a particular model will change on a case-by-case basis. Sources of uncertainty are most commonly related to inadequate physical characterization of the aquifer rather than the chemical analysis of the groundwater (Keely, 1983).

b. Numerical models: Numerical models require more input data than analytical models, and under some conditions possess a potential for more extensive data output. Numerical models break up functions of interest into many smaller units. The mathematical solutions that follow involve the

TABLE VI-3

ILLUSTRATIVE INPUT AND OUTPUT PARAMETERS FOR AN ANALYTICAL GROUNDWATER MODEL: THE PESTAN/PLUME MODEL

Input Parameters

Boundary conditions

- Maximum and minimum depths (unsaturated zone)
- Observation point coordinates (saturated zone)

Hydraulic variables

- Bulk density of soil
- Porosity of soil
- Aquifer porosity
- Solubility of contaminant
- Sorption constant in soil
- Degradation rate coefficient in soil
- Recharge rate
- Dispersion coefficient in soil
- Seepage velocity in aquifer
- Retardation coefficient in aquifer
- Dispersion coefficients for x- and y-axis
- Decay constant in aquifer

Concentration variables

- Maximum and minimum times
- Time duration of waste release (unsaturated zone)
- Frequency of waste release (unsaturated zone)
- Active ingredient released
- Mass rate and time
- Steady-state source rate

Other

- Curve coefficient
- Coordinate system
- Units
- Time

Output Parameters

- Water content of unsaturated zone
- Pollutant velocity in unsaturated zone
- Length of pollution slug in unsaturated zone
- Depth increments in unsaturated zone
- Solution concentrations in unsaturated zone
- Solid phase concentrations in unsaturated zone
- Total concentrations in unsaturated zone
- Concentration distribution matrix in aquifer at times desired for steady-state

Source: Enfield et al., 1982 and Wagner, 1982.

reduction of partial differential equations to algebraic equations which, in turn define the values of interest within each subdivision of the given function. In order for this method to approximate reality closely, the functions under study must be subdivided into as many discrete units as possible. As the number of small units in the model increases, the mechanics of performing the necessary mathematical calculations also become more complex.

There are several different forms of numerical models, but the two most common ones are referred to as finite-difference approaches and finite-element approaches. With both systems, continuous functions are approximated by a series of discrete equations in time and space which correlate with parameters of interest at reference points (nodes) or areas (nodal areas or elements) within a reference grid. The difference between finite-difference and finite-element methodology lies in the manner in which the original partial differential equations are reduced to algebraic expressions. In the finite-difference models, the mechanism is a differential approach; in the finite-element models, the mechanism is an integral approach.

The individual grid units may be either two or three dimensional; they can be square, rectangular, triangular, polygonal, or corresponding three dimensional shapes. All grid units within a single model usually maintain the same shape. Grid unit size, however, often varies within a model. For complex areas of the aquifer under study, a greater number of grid units per area or per volume may be designated.

Data requirements for the use of numerical models are very similar to the boundary condition, hydraulic variable, and concentration variable parameters mentioned earlier for analytical models. However, numerical models are designed to go beyond the scope of the analytical models and to generate more detailed, informative outputs, e.g., to account for a greater number of attenuating factors and complex aquifer boundary conditions. To achieve these objectives, numerical models require a commensurate increase in baseline data.

The input-output parameters for numerical models are similar from model to model, but there are variations reflecting different modeling approaches and unique features. For purposes of illustration, Table VI-4 presents an input-output breakdown for the Random Walk Solute Transport Model or TRANS (Prickett et al., 1981). This numerical model is widely recognized among hydrologists and is regarded by some authorities as among the best available for many solute transport modeling applications (Keely, 1983).

Numerical models can be used to model groundwater transport of hazardous waste in a wide variety of circumstances. From a technical standpoint, these models have the maximum modeling capability available. The factors which limit the use of numerical models include availability of trained personnel, computer facilities, substantial field data, and allocation of time and funds. Such models would not be appropriate for routine use, but would be very valuable in the study of isolated, high priority cases.

TABLE VI-4

ILLUSTRATIVE INPUT AND OUTPUT PARAMETERS FOR A NUMERICAL GROUNDWATER MODEL: THE RANDOM WALK SOLUTE TRANSPORT MODEL, TRANS[a]

INPUT PARAMETERS

Boundary Conditions

- Elevation of bottom of aquifer
- Default value for bottom of aquifer elevation
- Elevation of top of aquifer
- Heads at end of time increment
- Default value for heads
- Head at start of time increment
- Elevation of bottom of streambed or elevation below which evapotranspiration ceases
- Elevation of land or stream surface
- Default value for elevation of streambed bottom or elevation below which evapotranspiration ceases
- Default value for elevation of land on stream surface

Hydraulic Variables

- Actual porosity
- Effective porosity
- Hydraulic conductivity of aquifer
- Bulk mass density
- Storage conditions for artesian conditions
- Storage conditions for water table conditions
- Default value for storage values
- Aquifer transmissivity
- Longitudinal dispersivity
- Transverse dispersivity
- Vector retardation factor
- Array containing components of vector velocities
- Distribution coefficient
- Tensor component for hydraulic conductivity

Concentration Variables

- Concentration at the source
- Particle mass
- Constant withdrawal rates
- Default withdrawal rates
- Recharge factor
- Default recharge factor
- Volume of water to be accounted for before next particle is emitted

Other input Data

- Array used in system subroutine call
- Peaceman-Rachford B array
- Time increment in which particles are allowed to move
- Model grid interval in the x- and y-direction
- Spatial increment added to x- and y-coordinate over which particles will be placed or moved
- Peacemen-Rachford G array
- Logical unit number for input x- and y-coordinate of pump
- Table of sink coordinates
- Maximum number of particles in system
- Number of columns in model
- Total number of particles in system
- Number of random walk time steps per flow time step
- Number of pumps in system
- Number of rows in model
- Number of rates in pumping schedule
- Number of time increments per pumpage change
- Number of time increments
- Logical unit number for output
- Temperature variables

OUTPUT PARAMETERS

- Input parameters
- Values of heat at time steps
- Map showing concentrations
- Map showing number of particles residing in the model grids
- Particle mass
- Number of particles in system
- Sink locations

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[a] Prickett et al., 1981.

The numerical models do exhibit inherent minor sources of mathematical instability known as numerical dispersion or numerical oscillation (Mercer and Faust, 1981). However, with proper management, errors from these uncertainties are negligible (≤ 10%) compared to uncertainties introduced by input parameters (EPA, 1982a). In this regard, the comments on uncertainty in the analytical model discussion apply here as well. The margin of error in model output for verified, established models listed in this section varies from case to case, based on input error. Characterization of the aquifer properties, processes, and boundaries presents the greatest difficulty. If incorrect parameters are applied to a numerical model, the complexity of the model will serve to multiply the errors and an erroneous output profile will result.

No developing methodology was identified which would radically improve or replace the solute transport models described in this section. The greatest potential for increasing the accuracy of groundwater model outputs lies in improving the quality and quantity of input data describing aquifer properties and boundaries.

c. Summaries of mathematical models: Capsule descriptions of analytical and numerical models follow.

AT123D: The Analytical Transient One - Two - or Three - Dimensional code is a versatile tool for modeling the transport of wastes in aquifers with minimal input data. Developed for the Department of Energy by Yeh (1981) at ORNL, it can be applied to instantaneous, extended period or continuous releases from chemical or radioactive wastes and heat flows. It can address eight source configurations (point; 3 linear; 3 planar; and volume), four variations of aquifer depth and width, and transport parameters of advection, hydrodynamic dispersion, adsorption, degradation or decay, and volatilization to the atmosphere. Boundary conditions can include Dirichlet, Neumann, mixed type, and radiation. It is written in FORTRAN for IBM and DEC systems. It is well-suited to modeling hazardous waste transport from land disposal sites.

BIOFILM: This model is applicable in transport studies where biological films are the controlling factor in uptake and microbial degradation of low concentrations of organic chemicals from aqueous solutions. Developed by Rittman and coworkers (1980) at Stanford University for the U.S. Environmental Protection Agency, BIOFILM has been applied to land disposal of aqueous wastes as well as to conventional trickling filters in waste water treatment plants. BIOFILM contains both steady-state and non steady-state models. The former is based on Monod kinetics for substrate utilization, molecular diffusion for substrate transport within the film, and liquid-layer mass transport of substrate from bulk liquid to the film. It predicts substrate flux into the film as a function of its concentration in the bulk liquid and the thickness of the film for a given concentration of substrate. The nonsteady-state model can predict substrate flux into an existing film formed at a different concentration of substrate. The model is written in WATIV FORTRAN.

CFEST: The Coupled Fluid, Energy and Solute Transport model was developed by Battelle Pacific Northwest Laboratories for the U.S. Department of Energy's Underground Energy Storage Program (Gupta et al. 1982). Developed particularly for prediction of a confined aquifer's response to thermal energy storage, CFEST has also been of interest to the U. S. EPA for study of hazardous wastes disposed in landfills. It uses the finite element method for fluid flow, and has two- and three-dimensional applications. It has been verification-tested against analytical and semianalytical solutions. CFEST can be compiled with a one dimensional model developed by the same organization for the unsaturated zone UNSAT1D (Battelle, 1982) CFEST is available in FORTRAN and FLECS languages and is operational on the DEC PDP 11/70.

FEMWATER/FEMWASTE: These are affiliated Finite Element Method codes for Water and Waste constituents. Both use a Gaussian elimination solution technique and are two dimensional models that simulate groundwater dynamics in unsaturated-saturated porous media. Developed by Yeh and Ward (1980, 1981) for Oak Ridge National Laboratory, these state-of-the-art codes can be used either separately or in tandem. FEMWATER can include response of the groundwater basin to precipitation, pumping and other recharge/discharge effects. FEMWATER is sensitive to the grid discretization and soil characterization at sharp moisture fronts or vertical media interfaces (BPNL, 1984). FEMWASTE uses an advection-hydrodynamic dispersion equation to model solute transport. It can include chemisorption and first order decay. FEMWATER/FEMWASTE are written in FORTRAN and operational on both CDC and IBM 360 systems.

FIESTA: The Finite Element Solute Transport Model attempts to couple the effects of geochemical processes with solute transport. It is a one-dimensional model for transport of up to six component chemicals in the saturated zone. FIESTA was developed by Theis and coworkers (1982) at Notre Dame University for the Office of Health and Environmental Research of the U.S. Department of Energy. It combines elements from earlier models for transport and chemical speciation equilibria. It uses the finite element method for transport and Newton-Raphson technique for geochemistry. The model assumes homogeneous, isotropic soil systems and includes transport factors of dispersion and convection and chemical factors of nonlinear ion exchange, adsorption, and complex formation in solution. It is written in FORTRAN and operates on a CDC system or DEC VAX 11/780.

McWhorter-Nelson Hydraulic Model: McWhorter and Nelson (1979) provided a hydraulic expression useful for modeling selected applications in the unsaturated zone that do not require consideration of adsorption or attenuation interactions. It can provide the time to breakthrough to groundwater for leachate from a land disposal site.

MINTEQ: The MINTEQ code is one of several geochemical codes designed primarily for calculations of chemical equilibria in aqueous systems. It was developed at Battelle Pacific Northwest Laboratories for the U.S. Environmental Protection Agency (Felmy et al., 1983). MINTEQ combines the better features of earlier geochemical codes and a very large, documented thermodynamic data base to permit modeling of fairly complex systems involving metallic elements. It is capable of addressing ion speciation, activity coefficients, adsorption, precipitation, dissolution, ion exchange, and generation of gaseous O^2 and CO^2. It employs the Newton-Raphson numerical technique and is written in FORTRAN for the UNIVAC 1144 and DEC 11/70. A version is also available for the IBM PC XT or AT and compatible microcomputers.

NRC-SLB: The U.S. Nuclear Regulatory Commission's Shallow Land Burial model is a one-dimensional numerical code designed to compare the fate of contaminant from low-level radioactive wastes disposed under alternative scenarios in near-surface sites. The NRC-SLB's unsaturated zone submodel uses the finite difference method and its saturated zone submodel uses an analytical solution technique. The distribution coefficient (K_d) or retardation equation approach is used to model groundwater attenuation mechanisms. It also contains wind erosion and atmospheric dispersion components. The model can provide either a maximum individual dose or an integrated population dose over 50 years for comparison of scenarios. The model was developed for NRC's Division of Waste Management by Science Applications, Inc. (drawing on a flow model of Hanks and Childs) and is written in FORTRAN IV (Lester et al., 1981).

PATHS: This two-dimensional, semianalytical code was designed to make an initial and fairly rapid prediction from limited data of the transport of groundwater contaminants accidentally released from a storage facility to a predetermined boundary. Developed for the Department of Energy and the Electric Power Research Institute by Nelson and Schur (1980) at Battelle Pacific Northwest Laboratories, the code uses an idealized solution for the groundwater potential distribution and generated pathline differential equations to give the paths of fluid particles and their advance with time. The model has been applied to surface, near-surface and deep cavern storage problems (BPNL 1984). The program is written in FORTRAN-77 for the Univac 1100/44 and DEC VAX 11/780 systems.

PESTAN: This analytical model was developed by the EPA's Kerr Environmental Research Laboratory in Oklahoma to evaluate the transport of organics applied to land through the unsaturated soil zone to ground water (Enfield et al., 1982). PESTAN includes three different models: (1) linear adsorption/desorption of the pollutant without dispersion. (this mode can include first order microbial transformation); (2) a mode similar to the preceding, but with dispersion included; and (3) nonlinear adsorption following a Freundlich equation without dispersion with first order degradation.

PLUME: This is a solute transport model based on steady state two-dimensional advection-dispersion equation containing adsorption and degradation terms (Wagner, 1982; Bumb et al., 1984). Roy and Griffin (1987) used the PLUME model to estimate groundwater contamination by representative organic solvents leaking from solid waste at a hypothetical landfill site, and to estimate the threshold quantities of each that might be acceptably placed in the landfill under various assumptions of attenuation by dilution, adsorption, dispersion or degradation.

Plume Management: (or Wilson-Miller): This is a two dimensional analytical model (Wilson and Miller, 1978; Miller, 1978; USGS, 1981). It assumes a continuous point source, but nonsteady state conditions. It can yield estimates of concentration in the groundwater higher than the solubility limit for some constituents in the hazardous waste. Hunt (1978) developed a three-dimensional model for a continuous point source as well as a model for a pulse source of contaminant.

PRZM: The Pesticide Root Zone Model (Carsel et al., 1982) was developed by the EPA's Kerr Environmental Research Laboratory to predict the movement of surface-applied or surface-incorporated pesticides in or below the plant root zone. PRZM should be applicable to the transport and degradation in the unsaturated zone of other organic chemicals with linear adsorption behavior and first order kinetic reactions. The soil column is divided into several layers, mass balances are maintained for water and chemicals in each layer, and hydrologic factors include rainwater, runoff, snow accumulation/melting, evapotranspiration and percolation. PRZM uses a numerical solution to the advective dispersive equation for chemical transport, first order reversible sorption, and first order lumped decay kinetics (which can include microbial degradation). It can take into account both plant uptake and runoff losses of chemicals. PRZM can be used on microcomputers compatible with the IBM PC XT/AT systems.

SESOIL: The Seasonal Soil Model was designed for rapid evaluation of solute transport in the unsaturated zone of pollutants at waste treatment and disposal sites. It is a semianalytical (statistical/mathematical) compartmental model that, with minimal data requirements, can simulate waterflow and pollutant concentrations in a three-compartment soil column extending from the surface through the unsaturated zone. SESOIL uses a mass balance formulation and addresses seasonal variation in water, sediment and pollutant cycles. It averages the soil properties of the three compartments and yields a steady state moisture level with depth. It can take into account convection, diffusion, volatilization, adsorption/desorption, complexation of metals by organics, chemical degradation (hydrolysis, oxidation and photolysis), and biological uptake/transformation, (but not specifically plant uptake). SESOIL was developed by Arthur D. Little, Inc., for EPA's Office of Toxic Substances and is in FORTRAN (Bonazountas and Wagner, 1981). Because of SESOIL's emphasis on solutes and hydrogeological simplicity, it may not simulate short term response of the soil column to moisture levels as well as some other hydrological models.

SWIFT: The Sandia Waste Isolation Flow and Transport code is a three-dimensional finite difference groundwater flow and solute transport numerical model. Developed for the Nuclear Regulatory Commission by J. E. Campbell at Sandia National Laboratories (Dillon, Lantz and Pahwa, 1978), SWIFT was designed to take into account both mass and heat flows in modeling radionuclide transport with decay to daughter products in an isothermal or heated porous medium. The program is written in FORTRAN for the CDC 6600 system.

SWIP2: The SWIP model was developed to evaluate the effects of liquid wastes in deep saline aquifers in the design and testing of waste disposal systems. It is a transient, three-dimensional numerical model using a finite difference solution to the mass pressure and energy equations. Developed for the U.S. Geological Survey by INTERA Environmental Consultants, Inc., the original 1976 version was subsequently updated as SWIP2 by modifications to include free water surface, vertical recharge, equilibrium-controlled linear adsorption and an irreversible first order rate for simple chemical reactions (INTERA, 1979). The SWIP2 version is preferable for most hazardous chemical waste disposal applications. The program is written in FORTRAN for the CDC system and is available from the National Technical Information Service. SWIP is a subsystem in the EPA's GEMS model.

TRANS; Random Walk Solute Transport Model: Transport of a large class of solutes in groundwater can be simulated in this numerical model developed by Prickett, Naymik and Lonnquist (1981) for the Illinois State Water Survey. It applies a finite difference method to ground water flows, and "particle-in-a-cell" and "random walk" tracking techniques, respectively, to model solute convection and dispersion effects. TRANS can simulate in either one or two dimensions both steady or nonsteady flows in heterogenous aquifers under water table, artisan or leaky artisan conditions, and can handle exchange with surface water and evapotranspiration. An ability to simulate solute transport while ground water pumpage is underway is an important consideration for hazardous waste studies. The code allows specification of concentrations of chemical constituents in any segment of the model, and can accommodate chemical reactions and mixing of waters having different solute concentrations. This model is widely recognized by hydrologists, and is regarded by some authorities as among the best available for many solute transport modeling problems (Keely, 1983).

TRUST/MLTRAN: This multidimensional numerical code models water content, pressure distributions and flow in the unsaturated-saturated environment, using the kinematic pathline subroutine, MLTRAN. TRUST is based on the integrated finite difference method and an interactive explicit/implicit point solution technique. The model was developed primarily from an engineering perspective by Narasimhan and Witherspoon (1977) for the Department of Energy and updated by Reisenauer et al., (1982) for the Nuclear Regulatory Commission. TRUST does not differentiate solute effects. It has been used to analyze uranium mill tailings disposal (BPNL, 1984). TRUST is written in FORTRAN and can be operated on both CDC and DEC VAX 11/780 computers.

UNSAT1D: This one-dimensional numerical model is designed to simulate short-term water flows and chemical transport in the unsaturated zone, including infiltration, vertical seepage, and uptake by plant roots as functions of the-hydraulic properties of the soil. It requires information on precipitation/irrigation rates and frequency, evapotranspiration, soil properties and layering, and root growth characteristics. UNSAT1D contains a series of programs run in succession. It does not contain a solute transport component. It uses an implicit finite difference method and a Gaussian elimination solution technique, is written in Fortran, and was developed by Battelle for the U.S. Department of Energy and the Electric Power Research Institute (Bond et al., 1982).

USGS-MOC; Solute Transport and Dispersion Model: This model was developed by the U.S. Geological Survey to simulate the concentrations of dissolved chemicals in an aquifer at specified points and times under advection-dominated flow conditions (Konikow and Bredehoeft, 1978). It is sometimes called the USGS-MOC model because it uses the method of characteristics for solute transport; it uses the finite difference method for groundwater flow approximation. It can be applied to either one or two dimensional analysis of transient or steady state flow conditions and considers convective transport, hydrodynamic dispersion and mixing/dilution with other fluids in a heterogeneous or isotropic aquifer. It is designed for use on uniform grids and assumes that velocity distribution is not affected by gradients in fluid temperature, viscosity or density. Updated versions of MOC are said to be able to address solute adsorption and decay reactions. The U.S. EPA has examined MOC in studies of hazardous waste sites. It is written in FORTRAN for the CDC system.

VHS (Vertical and Horizontal Spread) Model: The VHS model is under development by the EPA Office of Solid Waste's Delisting Program to help determine if given industrial wastes might pose hazards to human health or the environment if disposed in an unlined landfill, based on a "Reasonable Worst Case" scenario for groundwater contamination. The model is adapted from Domenico and Palciauskas's (1982) VHS analytical model for predicting maximum plume concentrations, based on one dimensional steady flow and dispersion in directions perpendicular to the flow path.

The VHS model assumes: A landfill trench (40 ft x 8 ft) with a stated waste volume and measured leachate concentration; a continuous, steady velocity flow of contaminate to an aquifer; and 5 ft penetration of the leachate into the aquifer at the landfill boundary. The contaminant plume moves directly toward a receptor well 500 ft away at a groundwater dispersivity of 2 m/year (i.e. travel time for contaminants is 76.2 years). The model assumes only traverse (i.e. vertical and horizontal) dispersion. It does not consider: longitudinal dispersion; constituent attenuation by saturated soil, sorption, or chem/bio degradation; recharge dilution; or restriction of verticle spreading by any low permeability materials.

The VHS model has not been validated to date. It use for regulatory purposes has drawn serious criticism, and its future utility is uncertain.

VTT/MMT1D: The Variable Thickness Transient fluid flow model was developed for application to multiaquifer groundwater systems with transfers under pressure between aquifers, or an aquifer and a surface water body. VTT was developed by Battelle Pacific Northwest Laboratories for the Department of Energy, with particular consideration of conditions affecting waste disposal at the Hanford Site in Washington (Kipp et al., 1976; Reisenauer, 1979) and was recently updated by the Electric Power Research Institute (Bond, 1981). VTT is a flexible two dimensional model using one finite difference method for steady state conditions and a second version for transient conditions. The model can handle heterogeneous parameters, a variety of boundary conditions and configurations, and confined and unconfined aquifers. The VTT must be coupled with a solute transport model for predicting pollutant migration. The MMT1D, a random walk convective-dispersive transport model (Ahlstrom and Foote, 1976; Ahlstrom et al., 1977), or the MLTRAN subroutine with kinematric pathline approach are suitable (BPNL, 1984). The VTT is written in FORTRAN for the CDC system.

2. Ranking models: Contamination ranking models and the groundwater related portions of more general hazardous waste site ranking models, although not strictly groundwater transport models, might be valuable in cases involving potential hazardous waste emergencies. They may provide the only immediately available way to estimate potential groundwater problems, if the use of mathematical models must wait until substantial sampling and analysis are completed to provide necessary data. Ranking models could provide the best method available for scoping the problem and developing emergency response plans (Keely, 1983).

Ranking models are standardized schemes which permit an experienced observer to judge approximately the hazards presented by a particular problem site. Examples include the current forms of the LeGrand model (LeGrand, 1980 and Pettyjohn et al. 1981), the MITRE system, (OTA, 1983) and the JRB model (Kufs et al., 1980). A brief discussion of the LeGrand model will help to describe this group.

The LeGrand ranking system is based on four geologic and hydrologic characteristics:

1. Distance to a water supply;
2. Depth to water table;
3. Hydraulic gradient; and
4. Permeability-sorption (indicated by the geologic setting).

Each of these characteristics is evaluated and rated according to standard scales. For the water supply, water table, and permeability-sorption characteristics, a ranking scale of 0 to 9 is used; for the hydraulic gradient, a scale of 0 to 5 is employed. The ranking scale for distance to a water supply ranges from 0 for distances in excess of 6,200 ft to 9 for distances of up to 45 ft. The depth of the water table scale ranges from 0 for depths in excess of 200 ft to 9 for depths of 0 ft (surface water). The permeability-sorption scale is more complex and depends on the type of soil and the thickness of unconsolidated materials over bedrock. For the water table gradient scale, a low value of 0 is assigned if the gradient is away from all water supplies closer than 1,000 m; a high value of 5 is assigned for gradients greater than 2% towards the water supply. The arithmetic sum of the rankings for the four characteristics will fall somewhere in a range from 0 to 32, 0 representing the safest end of the spectrum and 32 representing the most hazardous. Letter rankings (A through D) are added also to indicate permeability-sorption, level of confidence, nature of the closest water supply, and a final designation for the most appropriate of 11 site descriptions (a fifth letter may also be included if two of these descriptors apply). The final product is a series of numerals and letters which provide a yardstick for preliminary ranking purposes.

Other ranking methodologies vary in features, but the concepts are similar. All such procedures require minimal data input, equipment, time and expense, and yield quasi-quantitative site evaluations. Data needs for ranking models are less rigorous than the corresponding inputs required for mathematical models. The modest data requirements of ranking models make their use easier in the field than analytical or numerical mathematical models. There are, however, disadvantages in the use of ranking models, including the lack of definitive quantitative output (e.g., potential contaminant concentrations at a postulated point of human contact) and the inability to allow for complex physical, chemical, and biological factors. Because ranking models have no calculated outputs comparable to analytical or numerical models, identification of mathematical margins of error are not possible.

C. Surface Water Models

Studies of environmental contaminants in surface waters are generally divided into two categories: (1) dispersion in streams, etc., of pollutants that are discharged, spilled or otherwise released at a point source; and (2) runoff of pollutants from a land surface area into streams following precipitation (i.e., nonpoint watershed runoff studies). Watershed runoff is generally a minor problem compared to other transport routes for hazardous waste management, although it is important in other environmental studies such as pesticide or fertilizer impacts. Numerous mathematical models have been developed for both kinds of studies.

1. Pollutant dispersion models: Dispersion models are used to predict the dispersion and fate of chemicals discharged or spilled into streams, rivers, lakes, estuaries, or oceans. A stream or river is modeled as a series of completely mixed reaches. Steady-state contaminant concentrations in each are then estimated based on dilution and physical/chemical removal of contaminants from the water column. Several dispersion water models of different types and complexities are available (Onishi et al., 1980b; Burns et al., 1982; Browman et al., 1982; DiToro et al., 1981; Onishi, 1985a, 1985b; and Schnoor, 1985).

The model most widely used to compute fate, persistence, and exposure of pollutants in freshwater ecosystems is EXAMS (Exposure Analysis Modeling System) which was developed by EPA's Environmental Research Laboratory at Athens, Georgia. Other models which have been used for surface water pollutant dispersion studies include: TOXIWASP; SLSA; and QUAL.

EXAMS is designed for the rapid screening and evaluation of the behavior of synthetic organic chemicals in aquatic environments (Burns et al., 1981, 1982). The model requires three types of data: chemical, environmental, and loading rates. Chemical data requirements include physical constants (e.g., molecular weight, solubility) and parameters to compute transformations such as photolysis, hydrolysis, oxidation, and biotransformation. EXAMS is interactively linked to a data base of properties of chemicals. Environmental data requirements include system geometry, hydrology, and meteorology, and definition of dispersive and advective pathways for both water and sediments. EXAMS can partition pollutants among five valence states and three physical forms (adsorbed, biosorbed, and dissolved). Pollutant loadings can be specified as point source, nonpoint source, dry fallout or aerial drift, atmospheric washout, and groundwater seepage. Processes such as photolysis, hydrolysis, oxidation, volatilization, and biotransformation are simulated as pseudo first-order kinetic reactions. Second-order effects can be introduced also. EXAMS does not handle dynamic (transient) flow conditions, its hydraulic and sedimentation algorithms are limited, and it is limited to organic chemicals. Field validation results have been reported (Games, 1982). A version of the EXAMS model is available for use on microcomputers compatible with IBM PC XT/AT systems.

TOXIWASP is a kinetic subroutine for the Water Analysis Simulation Program (WASP; see DiToro et al. 1981) and was also developed by EPA's Environmental Research Laboratory. The toxics degradation techniques from EXAMS are simplified by adding the pseudo first-order rates due to photolysis, oxidation, biolysis, hydrolysis, and volatilization to yield a total degradation rate. TOXIWASP calculates the dissolved, sorbed, and biosorbed fractions of a neutral chemical only. It has the capability to simulate dynamic as well as steady-state wasteloads. As in EXAMS, laboratory and literature values for the chemical characteristics of a compound may be used. WASP3 is available for use on IBM PC/XT and compatible microcomputers.

SLSA (or HydroQual Model) is a simplified model developed by HydroQual, Inc. and the Chemical Manufacturers Association for the study of the fate of partitioning chemicals in lakes and streams (DiToro et al., 1982). Total degradation rate of a substance is estimated by adding the pseudo first-order rates due to the kinetic processes, as in TOXIWASP. Mechanisms considered are settling, resuspension, and diffusion. The adsorption-desorption reaction is assumed to be at equilibrium. The fraction of the chemical mass that is either dissolved or adsorbed to particulates is determined by the mass of the adsorbing solid and the partition coefficient in the water column and in the sediment. Treatment of column-sediment interactions is a strong feature of the model. All algebraic and differential equations are expressed in a form as simplified as possible. Closed form solutions, based on the conservation of mass, are presented and operated on a minicomputer linked into graphics output devices.

QUAL was designed to simulate spatial and temporal variations of dissolved oxygen, biological oxygen demand, up to three conservative minerals and temperature in stream and canal systems under steady-state flow conditions. The model is actually a set of interrelated quality routing models based on empiric and kinetic considerations. Developed originally as QUAL-I in 1970 by the Texas Water Development Board (TWDB, 1970), the model was improved (QUAL-II) under EPA support (NRRC, 1974), but is less favored now than newer, more versatile models. The QUAL2E version can be used on the IBM PC XT/AT family of microcomputers and compatible systems.

Other Models: According to Travis (1985) most currently available methods for evaluating dispersion of contaminants in streams do not account adequately for sediment transport. Such models must calculate time-varying distributions of contaminant adsorbed by sediment for each sediment size fraction. He indicated that the most advanced two-dimensional models of this type are SERATRA (vertical and longitudinal) (Onishi and Wise, 1979; Onishi et al., 1980b) and FETRA (lateral and longitudinal) (Onishi, 1981).

2. Watershed runoff models: Watershed models are used to predict the quantity and quality of water that (after falling as rain) flows off of the land surface into receiving streams carrying dissolved and suspended materials. Over 80 different runoff models are said to be available; they have different input requirements and address many different aspects of the problem. Only 12 of these models, however, simulate both dissolved and sediment-sorbed migration together with the surface runoff and soil erosion processes (Onishi, 1985b; Travis, 1985).

Two broad classes of watershed runoff models exist: (1) those that focus almost entirely on the quantity of runoff water; and (2) those that emphasize information on the quality of runoff water, i.e., the environmental contaminants. (Nearly all watershed models simulate erosion rates.) Runoff models are sometimes classified also according to operational characteristics, including geometrical representation of the drainage basin, temporal representation of flow, and physical process representation, each of which has subsets as noted below:

- Geometrical Representation (lumped or distributed):

  - *Lumped models* represent the drainage basin as a whole, without detailed spatial characterization of subbasins or without the spatial distribution of contaminants within the drainage basin.

  - *Distributed models* represent the drainage basin on a grid or map basis, and accounts for variations in hydrologic processes and contaminant distributions from point to point throughout the basin.

- Temporal Representation of Flow (continuous or discrete):

  - *Continuous simulation models* describe a time series of runoff flow and runoff quality within the drainage basin over an extended period, e.g., 1 year.

  - *Discrete storm event models* describe the basin response to a single storm (runoff-producing event), but may describe that response in summary (storm-averaged) form. Most runoff and erosion from a drainage basin over a long period of time are concentrated in a few storm events; discrete models use this simplification in their simulations and as a result are more widely used than continuous simulation models.

- Physical Process Representation (descriptive or conceptual):

  - *Descriptive models* use basic physical parameters to account for observed phenomena. They have the greatest use by practicing hydrologists.

  - *Conceptual models* rely heavily on theory to interpret phenomena rather than to represent the physical process (i.e., these models are based on probability theory).

Described below are several general features of runoff models, and then specific runoff quantity and runoff quality models.

a. *Features of runoff models*: Runoff models focus on interactions at the soil surface such as overland flow, sediment transport, and sediment and water quality. (Some can simulate subsurface pollutant migration pathways also.) Runoff models are designed to estimate delivery of nonpoint source pollutants to streams and other bodies of surface water in a region. In order to estimate pollutant loads, watershed models first describe the hydrologic characteristics of the watershed, such as soil moisture and groundwater recharge, followed by watershed sediment loads, and finally watershed chemical characteristics. The number of soil chemical phenomena and the sophistication of chemical processes simulated vary widely among models. Many watershed models, however, incorporate the same or similar hydrologic algorithms.

Some of the approaches used for hydrological processes involve parameters which are not directly observable, such as water infiltration rate. The further a model deviates from fundamental physical laws or relies on parameters which are not directly observable, the less likely it is to be useful in a general application to watershed modeling. The models most suitable for simulation of contaminant migration require extensive site-specific data for calibration of the model (Basta and Bower, 1982).

A number of environmental factors influence the quantity of runoff, and many physical and chemical processes affect its quality. These factors and processes interact to form nonpoint source pollution and should be considered in watershed modeling. From a data needs standpoint these factors and processes can be divided into three areas: hydrologic phenomena; erosion processes; and chemical processes.

Major hydrologic phenomena affecting quantity of runoff are: precipitation, infiltration, evapotranspiration, overland flow, interflow, groundwater recharge, and depression storage. These phenomena are all components of the hydrologic cycle.

Soil erosion is the most important process affecting quality of runoff. Erosion involves two steps: detachment of soil particles from the land surface and transport of these particles by overland flow. Because many contaminants adsorb to soil particles, soil erosion data are very useful in estimation of contaminant loads to surface water bodies. Efforts have been made to predict soil erosion as accurately as possible, but soil particle detachment is dependent upon a number of factors: particle cohesiveness; organic matter content of the soil profile; rainfall intensity; vegetative cover; slope gradient; slope length; and soil cultural practices (Wischmeier and Smith, 1978).

Many chemical processes have an impact on contaminant behavior because of the complexity of soil chemistry and the broad range of contaminants associated with runoff. Some processes frequently addressed by operational models include:

- Adsorption of contaminant to soil particles (usually characterized by a partitioning coefficient).
- Solubility of contaminants and of soil components.
- Volatility of organic compounds (may depend on meteorological conditions).
- Biodegradation of contaminants by soil microorganisms.
- Soil pH (influences contaminant solubilities).

- Redox potential of soil solution (influences mobility of metals).

Hence these models require detailed hydrologic, meteorological, and watershed data, together with the chemical and distributional properties of the contaminants. Several catalogs and handbooks exist that provide means of evaluating watershed models as well as other environmental models (Basta and Bower, 1982; EPA, 1982b).

b. Runoff quantity models: Five models are discussed below:

Rational Formula: The simplest of all hydrologic models is the Rational Formula, first introduced nearly 100 years ago. The simplicity of this method (and others derived from it) limits its application to situations where only a rough estimate of runoff is needed. It is best applied to calculate urban area runoffs. The rainfall-runoff formulas are difficult to apply unless the return periods for rainfall and runoff are assumed to be equal. Peak runoff rates are predicted by correlating flow rates with only simple drainage basin characteristics, such as area and slope. These correlative methods are limited in applications because they are derived from localized data and are not valid when extrapolated to other basins (Viessman et al., 1977).

Stanford Watershed Model IV (SWM-IV): SWM, one of the earliest and most comprehensive numerical models, is based on classical methods of hydrograph separation, i.e., identification of surface runoff, interflow, base flow, etc., from the observed time series of rainfall and total runoff. Many other models use SWM as a basis for determining nonurban, nonpoint source pollution. Calibrated input parameters are available for more than 100 watersheds around the nation. The model also considers snow melt.

U.S. Department of Agriculture Hydrological Laboratory Model USDAHL-74: This model is a physically based, distributed storm event model incorporating many phenomena known to influence runoff and erosion. The model demands specification of more input parameters than SWM, but relies less upon calibration versus observed hydrographs. It predicts rainfall from nonurban land areas.

Storage, Treatment, Overflow Model (STORM) (Corps of Eng., 1976) and the Storm Water Management Model (SWMM) (EPA, 1971) are fairly widely used, but simulate primarily hydrologic processes of water movement and do not estimate chemical transport directly.

c. Runoff quality models

Six models are regarded as being particularly useful in predicting quality of runoff. They cover a variety of runoff quality aspects. Brief descriptions of these models are given below and their characteristics are compared in Table VI-5. Onishi (1985b) and Donigian and Dean (1985) have compared some of these and several other watershed models according to processes simulated and land use.

TABLE VI-5

COMPARISON OF SELECTED WATER QUALITY RUNOFF MODELS

Model Name	Acronym	Use	Geometry	Time Scale	Hydrologic Submodel	Chemical Processes	Chemical Processes	Inputs[a]	Outputs[b]	Comments
Agricultural Runoff Management	ARM	Agricultural watersheds	Lumped	Continuous	SWM	No	Adsorption; linear decay solubility; nutrient cycle	Multiyear precipitation time series; calibration data	B	
Chemical Migration and Risk Assessment Methodology	CMRA	Risk assessment, toxic pollutants	Lumped	Continuous	SWM	Yes	Particle size dependent adsorption in channels; otherwise based on ARM	Multiyear precipitation time series; toxicity; channel geometry and bottom deposits characterization; calibration data	C	ARM-based runoff; sophisticated sediment transportation channels
Chemical, Runoff, and Erosion from Agricultural Management Systems	CREAMS	Agricultural watersheds	Lumped	Storm event	SCS (option 1) Green and Ampt infiltration based (option 2)	Yes	Particle size dependent adsorption linear decay; percolation retarded by adsorption; nutrient cycle; plant uptake	Daily or hourly rainfall	A	
Hydrological Simulation Program--FORTRAN	HSPF	Several land uses	Lumped	Continuous	SWM	Yes	Adsorption; linear decay; solubility nutrient cycle	Multiyear precipitation time series; calibration data	C	
Nonpoint Source Pollutant Loading	NPS	Variety of land uses	Lumped	Continuous	SWM	No	Adsorption (containment a fixed fraction of sediment)	Multiyear precipitation time series; calibration data	B	
Unified Transport Model	UTM	Esp. for metals and other pollutants deposited from air	Lumped	Continuous	SWM	Yes	Adsorption; linear decay; volatilization; plant uptake	Multiyear precipitation time series; atmos. dispersion parameters; calibration data	B	Include atmos. transport and deposition

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[a] Nearly all models, with the exception of NPS and NSPF require agricultural management practices; all require meteorological data; watershed, topographic, and solid characterization; and chemical application rates. Deviations from the norm are noted.

[b] A = Nonpoint source loads, storm summary; B = Nonpoint source loads, time series; and C = Stream quality, time series.

Agricultural Runoff Management (ARM): The ARM model predicts runoff, sediment, and contaminant loadings at the edge of a stream. It provides continuous simulation of contaminant loading by modeling hydrologic response of watersheds, soil erosion, contaminant adsorption and removal, and contaminant degradation (Donigian and Davis, 1978; and EPA, 1982b).

Chemical Migration and Risk Assessment Methodology (CMRA): The CMRA methodology predicts the occurrence and duration of toxic contaminants in stream systems. At the same time, it predicts the probability of acute and chronic damages to aquatic biota. The methodology consists of the following components: (a) overland contaminant transport modeling; (b) instream contaminant transport modeling; (c) statistical analysis of instream contaminant concentrations; and (d) probabilistic risk assessment. (Onishi et al., 1980a).

Chemicals, Runoff, and Erosion from Agricultural Management Systems (CREAMS): CREAMS is the U.S. Department of Agriculture's latest watershed model for estimating runoff, erosion/sediment transport and nutrient/pesticide losses from the surface and root zone of fields. It incorporates two alternate hydrologic components. Option 1 represents minor modifications and computerization of the SCS curve number approach. Option 2 is a relatively sophisticated model requiring high frequency rainfall data. CREAMS routines can be characterized as physically based, lumped parameter models that produce total storm runoff and peak runoff rates. The input parameters are physically observable and may be estimated from findings on watersheds. (Knisel, 1980).

Hydrological Simulation Program - FORTRAN (HSPF): HSPF is a comprehensive simulation model for predicting watershed hydrology, water quality, agricultural chemical migration, and risk assessment. The simulation model uses such information as the time history of rainfall, temperature, and solar intensity and characteristics of the land surface such as land use patterns, soil characteristics, and agricultural practices to simulate the processes that occur in a watershed. Flow rate, sediment load, and nutrient and pesticide concentrations are predicted. The model takes these results, adds information about the stream channels in the watershed, and simulates the processes that occur in these streams. This part of the simulation produces a time history of water quantity, quality, and chemical transport at any point in a watershed--the inflow to a lake, for example. The model also contains a risk assessment methodology to evaluate lethal and sublethal effects using the median lethal concentration (LC50) and maximum acceptable toxicant concentration (MATC) as the key effects parameters (Barnwell, 1981; Donigian, 1981; Donigian et al., 1983; Johanson and Kittle, 1983; and Johanson et al., 1984).

Nonpoint Source Pollutant Loading (NPS) Model: The NPS model is a continuous simulation model that represents the generation of nonpoint pollutants from the land surface. The model continuously simulates hydrologic processes (surface and subsurface), snow accumulation and melt, sediment generation, pollutant accumulation, and pollutant transport for any selected period of input meteorologic data. The NPS model estimates the total transport of pollutants from the land surface to a watercourse. It does not simulate in-stream processes that occur after the pollutants are in the stream. The model uses mathematical equations that represent the physical processes important to nonpoint source pollution. The NPS model should be calibrated whenever it is applied to a new watershed. However, most NPS model parameters are specific by physical watershed characteristics and do not require calibration (Donigian and Crawford, 1976).

Unified Transport Model (UTM): The UTM simulates the transport of toxic trace metals through an ecosystem consisting of the atmosphere, land surface, vegetation, soil layers, groundwater, and streams (Munro et al., 1976). It operates with a time step of 1 hr when rain is absent and 15 min when it rains. The UTM is actually a group of models that may be configured, the output of one serving as input to the next, to yield a multimedia model. Different configurations of the UTM have been applied to watersheds ranging in size from about 2,000 sq km to the order of 10,000 sq km. Input data include vales for historical hourly precipitation, daily average wind speed, maximum and minimum temperature, dew point, and integrated total radiation. Values characterizing the watershed topography, soil characteristics, and vegetative cover also are inputs. A version applicable to organic chemicals (UTM-TOX) has been mentioned (Hedden, 1982, 1984).

D. Air Models

Air quality models may be divided into two broad categories: (a) statistical models, and (b) dispersion (or simulation) models. Statistical models require extensive actual atmospheric monitoring data (including air quality and detailed meteorological measurements) for the specific site. Transfer of the results from these models from location to location (without re-estimation of parameters) is difficult. Hence, statistical models are of quite limited value as potential components of a generic comparative risk assessment methodology and are not described further in this report. Recent reviews of mathematical models for air pollutants are available (EPA, 1978, 1981; Geraghty and Ricci, 1985; Khalic and Rasmussen, 1985).

Dispersion models attempt to simulate the physical processes of the transport and dilution of airborne pollutants.* These models are more applicable than statistical models in the present study for two reasons: (a) they provide a degree of similarity in the use of the models between sites, and (b) they do not require actual historical monitoring data for the specific site. The principal requirements are source emission rates and meteorological input consisting of wind speed, wind direction, and atmospheric stability. The model then predicts time-averaged concentrations at specific locations for these emission rates. These predictions are based on mathematical relationships using empirical data corresponding to the particular meteorological condition. This type of model does not attempt to describe instantaneous conditions but rather time-averaged conditions. Because they are developed in terms of fundamental physical principles of general applicability, simulation models have the important property of being transferable from one location to another (EPA, 1978). Dispersion models typically do not require monitored air quality data except to fix initial or boundary conditions, and for purposes of model calibration and verification.

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* Farmer et al. (1980) describe methods for predicting vapor movement through soils.

A large number of air models have been developed. Models considered here for the exposure assessment methodology were of two kinds: those approved by EPA and included in the User's Network for Applied Modeling of Air Pollution, or UNAMAP series (EPA, 1981); and the ATM developed by Oak Ridge National Laboratory, which is considered a "reference" model in the OAQPS Guidelines Series (EPA, 1978). The ATM has several features that make it potentially useful for dispersion modeling of toxic pollutants. The current UNAMAP package (UNAMAP-4) contains 21 models; they were developed for specific applications, but have many features in common. All the models can be classified as steady-state and semi-empirical, and are based on Gaussian plume concepts which assume that the plume disperses in the horizontal and vertical directions following a Gaussian concentration distribution. The differences between models arise primarily from variations in the treatment of: (a) plume rise, (b) pollutant half-life, (c) diffusion limitations due to mixing heights, (d) source configurations, and (e) the dispersion coefficients used to characterize plume growth.

Air dispersion models can be classed in three broad categories: (a) screening models; (b) refined models; and (c) specialized models. For most current regulatory problems, screening models are used in single analyses to determine maximum air quality impacts. The calculations are based on assumptions that tend to overestimate actual concentrations. Screening models also may be applied to large emission inventories as an aid to determining suitable levels of aggregation as well as to exclude insignificant sources prior to more refined analysis. The refined models are typically employed to determine air quality impacts in more complex situations. Refined models are necessary when the interaction of many sources must be analyzed. The specialized models category includes those that are approved by EPA for application only on a case-by-case basis.

Descriptions of 16 selected air models are given below, organized according to these three categories. These descriptions highlight some of the features and capabilities that differentiate the various models of the UNAMAP series. Most of the UNAMAP models have a published user's guide that provides a relatively complete technical description. In addition, more detailed model abstracts can be found in the EPA Environmental Modeling Catalogue (EPA, 1982b). Twelve of these models were selected for systematic analysis of their capabilities, as shown in Table VI-6. Following the model descriptions, criteria for model selection and the accuracy and limitations of models are discussed.

1. Screening models

Point Source Model (PTDIS): PTDIS is a historical model that may be used to define the isopleths (i.e., equal areas) of constant concentration from a single point source.

TABLE VI-6

CAPABILITIES OF REVIEWED AIR MODELS[a]

Model Function	Model[b] ATM	CDM(QC)	CRSTER	ISC	MPTER	PAL	PTDIS	PTPLU	RAM	TCM-2	TEM-8	VALLEY
Source type												
Point source:												
Single	X	X	X	X	X	X	X	X	X	X	X	X
Multiple	X	X	X[c]	X	X	X			X	X	X	X
Area source	X	X		X		X			X	X	X	X
Line source	X					X						
Volume source				X								
Averaging Period												
Short-term	X		X	X	X	X	X	X	X		X	X
Long-term	X	X	X	X					X	X		X
Pollutant Deposition												
Gravitational settling	X			X								
Half-life	X	X		X	X				X	X	X	X
Turbulent deposition	X											
Washout	X											
Particle resuspension	X											
Geographical												
Complex terrain												X
Terrain adjustment			X	X	X							
Urban/rural applications[d]	X	U	X	X	X	R	R	R	X	X	X	X
Other												
Aerodynamic effects		X		X	X							
Momentum plume rise				X	X				X	X	X	
Stack tip downwash				X	X		X	X	X		X	
Emission rates function of MET conditions				X								
Emission rates function of time of day				X								
σ_y Function of averaging time and stability												X
Inversion penetration factors											X	

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[a] Matrix includes only screening and refined model categories.

[b] ATM = Atmospheric Transport Model.
CDM(QC) = Climatologic Dispersion Models.
CRSTER = Single Source Model.
ISC = Industrial Source Complex.
MPTER = Multiple Point Gaussian Dispersion Algorithm
PAL = Point, Area, Line Source Algorithm
PTDIS = Point Source Model.
PTPLU = Point Source Gaussian Plume Model.
RAM = Gaussian Plume Multiple Source Air Quality Algorithm.
TCM-2 = Texas Climatological Model, Version 2.
TEM-8 = Texas Episodic Model, Version 8.
VALLEY = Gaussian Plume Dispersion Algorithm.

[c] Sources are treated as co-located.

[d] R = rural only; U= urban only; X = rural and urban.

Point Source Model (PTMAX): PTMAX is a historical model that has been superceded by PTPLU (see the following).

Point Source Gaussian Plume Model (PTPLU): The PTPLU model is an improved version of PTMAX. Applied to a single point source, it is useful as a screening model for quickly estimating maximum 1-hr ground-level concentrations and the distance to maximum concentrations for varying combinations of wind speed and stability class.

Point Source Model (PTMTP): PTMTP is a historical model that has been superceded by PAL or by using MPTER or ISCST with user selected meteorology.

Point, Area, Line Source Algorithm (PAL): The PAL model is an enhanced version of PTMTP that may be used to estimate short-term concentrations (1 to 24 hr) from point sources, area sources, two types of line sources, and two types of curved path sources. The algorithm is not intended for application to entire urban areas. It is suitable for small-scale analysis of the impact of a single industrial facility or for evaluation of fugitive dust sources.

Texas Episodic Model, Version 8 (TEM-8): TEM-8 was developed as an alternative to the PTMTP and PAL models. It may be used to estimate ground-level short-term (10 min to 24 hr) concentrations from point and area sources in flat or gently rolling terrain. TEM-8 differs from other models in the UNAMAP series in its ability to account for variability in the horizontal dispersion coefficients as a function of averaging time and stability. As an additional capability, it can yield more realistic treatments of plume restriction beneath an elevated inversion.

Texas Climatological Model, Version 2 (TCM-2): TCM-2 may be used to estimate long-term (seasonal or annual) ground-level concentrations in urban or rural areas (TACB, 1980).

Gaussian Plume Dispersion Algorithm (VALLEY): VALLEY is designed to estimate either 24-hr or annual concentrations in complex terrain. VALLEY and two other models (COMPLEX I and COMPLEX II, which are variations of the basic VALLEY algorithm) are the only UNAMAP models that will estimate concentrations at receptors located above the stack height. The COMPLEX models, however, are still under evaluation and have not been recommended for use by EPA. VALLEY's treatment of plume impaction in complex terrain has been criticized. However, it continues to be an EPA-approved option for screening air quality impacts in complex terrain. It should be noted that VALLEY does not consider the lee side effects created by significant terrain features, nor does it consider the potential impacts created by terrain-induced downwash. In general, the inherent difficulties associated with modeling pollutant dispersion in complex terrain limit the applicability of the VALLEY model.

2. Refined models

Single Source Model (CRSTER): This point-source model is designed to estimate ground-level concentrations due to emissions from up to 19 co-located, elevated stacks on an hour-by-hour basis for an entire year. CRSTER may be applied in rural and urban settings, and will consider uneven terrain as long as receptor elevations are not located above the lowest stack height. In addition to providing estimates of maximum hourly concentration for each day and 24-hr averages, CRSTER produces summary tables which include annual mean concentrations, and highest and second highest 1-, 3-, and 24-hr concentrations.

Gaussian Plume Multiple Source Air Quality Algorithm (RAM): This model is used primarily to estimate short-term (1 to 24 hr) concentrations from point and area sources in urban areas. It may be applied in four ways: urban short term, rural short term, urban full year, and rural full year. In all modes, hourly averages are the basic unit for calculating concentrations. The urban mode uses McElroy/Pooler dispersion coefficients, while rural applications will access the Pasquill-Gifford dispersion coefficients. Operating in the full-year mode, it is possible to compute cumulative frequency distributions based on 24-hr averages for up to 1 year of data at a limited number of receptors. There are no provisions in the RAM model to account for elevation differences between sources and receptors.

Multiple Point Gaussian Dispersion Algorithm (MPTER): MPTER is a multiple point source model that may be used to estimate hourly concentrations or averages over the time period covered by the input data. MPTER is very similar to the rural version of RAM. However, unlike RAM, MPTER is capable of adjusting for slight terrain variations by considering differences between source and receptor ground-level elevations. Receptor ground- level elevations cannot exceed the height of the lowest stack or be less than the lowest stack base elevation.

Climatological Dispersion Models [CDM and CDM(QC)]: These models may be used to estimate long-term (usually seasonal and annual) concentrations from point and area sources within an urban area. Two pollutants can be modeled simultaneously, with the option of user-specified half-life values for simulating plume depletion. CDM(QC) is applicable in areas of flat or gently rolling terrain. It also has a calibration package and the capability to produce individual source contribution lists, in addition to the capabilities of CDM.

Industrial Source Complex (ISC): The most flexible of the UNAMAP series models, ISC can be used in either short-term (ISCST) or long-term (ISCLT) versions for both urban and rural applications. It is applicable to point, area, and volume sources; the latter may be used to simulate line source type industrial process fugitives. A user's guide for the ISC is available (Bowers et al., 1979).

Some of ISC's potentially useful features are: (a) a procedure to simulate building wakes and stack tip downwash effects; (b) plume rise due to momentum and buoyancy as a function of downwind distance; (c) time- dependent exponential decay of the pollutant; and (d) the capability to simulate gravitational settling and dry deposition. ISC is the only model in the UNAMAP series that incorporates the latter feature. ISCLT is used as a component in EPA's Inhalation Exposure Modeling (IEM) system to link concentration modeling capabilities with computerized meteorological and population data bases (EPA, 1983a).

Atmospheric Transport Model (ATM): This model is designed primarily to provide long-term (e.g., annual average) estimates of concentrations and deposition of pollutants released from a point or diffuse source. (It can be used to calculate hourly estimates.) ATM has analytical capabilities to consider washout and turbulent deposition. It does not have some of the features of the more refined UNAMAP models, including: (a) stack tip downwash, (b) building wake effects, and (c) terrain adjustments. Representation of area and line sources is not as sophisticated as in many other UNAMAP models. ATMTOX (Atmospheric Transport Model for Toxic Substances), a gaussian plume model applicable to Mesoscale (0.1-50 km) studies, is used as the air component in the Unified Transport Model-Toxics (UTM-TOX) developed by Oak Ridge National Laboratory for the EPA (Hedden, 1984). It can be used to estimate annual average atmospheric concentrations and deposition values resulting from gaseous or particulate releases. The program is in FORTRAN and is available on magnetic tape from the National Technical Information Service (Kaufman and Kinerson, 1985a). The ATM is accessible also as a module in the EPA's multimedia Graphical Exposure Modeling System (GEMS), and can be combined with population data to calculate numbers of persons exposed at various concentrations.

3. Specialized models

COMPLEX I and II: COMPLEX I and II are very similar to the MPTER model except that they allow for consideration of terrain higher than the lowest stack height. Five options are available to address the interaction of a plume with terrain. The complex terrain group of the EPA Office of Air Quality Planning and Standards (OAQPS) at RTP suggested the algorithm for the COMPLEX models. The only difference between COMPLEX I and II is in estimating horizontal dispersion coefficients.

BLP: This model can estimate the plume rise and ground-level concentrations resulting from emissions from buildings by using roof monitoring data. It was developed specifically for the glass, aluminum, and graphite electrode industries, and its development was funded by the Aluminum Association.

BOXMOD80: This atmospheric area source model estimates concentrations within an area containing many diffuse emission sources (e.g., multiple sources, urban areas). It also retrieves 1980 population data to calculate exposure. BOXMOD is accessible as a module in EPA's GEMS network.

4. Criteria for model selection: In selecting a model(s) for a particular application, five general aspects of the problem should be considered. These are: (a) pollutant characteristics, (b) source type(s), (c) geographical or land-use characteristics, (d) data requirements, and (e) averaging period.

Pollutant Characteristics: Dispersion modeling of toxic air pollutants should consider numerous depletion processes (including wet and dry deposition and gravitational settling) that can vary with pollutant characteristics. Unfortunately, the physics of deposition processes is incompletely understood (EPA, 1981). The current UNAMAP models (designed primarily to estimate concentrations for relatively stable criteria pollutants such as suspended particulates) are capable of only a fairly simplistic representation of these processes, with the more refined models representing plume depletion as a function of a half-life term and travel time downwind. The ATM model differs from the most refined UNAMAP models in that it has the analytical capability to consider wet deposition, turbulent deposition, and particle resuspension. In most cases the lack of data available to specify deposition terms limits the usefulness of these features.

Source Type(s): Source type and source-receptor configurations are probably the most flexibly represented aspect of the UNAMAP series. Models are available to consider: (a) a single or limited number of point sources, (b) multiple point sources, (c) multiple point and area sources, and (d) more specialized representations including line and volume sources. In general, when the dimensions of a stationary source are small compared to the distance at which concentrations are to be estimated, the source may be treated as a geometric point. Hazardous waste treatment/disposal facilities subject to RCRA will generally fit this criteria, although a land surface disposal activity or a very large landfill might require treatment as area sources. (In practice, multiple close sources that emit small amounts of criteria pollutants are often aggregated and treated as uniformly emitting area sources since their number and highly variable emission rates preclude treatment as individual sources.)

Geographic and Land-Use Characteristics: Several geographical and land-use characteristics should be considered in selecting a model from the UNAMAP series (EPA, 1981). A primary consideration is whether the area of interest is predominantly urban or rural. Some of the models are applicable only to rural areas, others are appropriate only for urban areas. Some of the more refined models are both urban and rural (options with the primary differences in the two modes being (a) the choice of dispersion coefficients used to characterize the plume behavior, and (b) the treatment of meteorological parameters such as atmospheric stability and mixing heights). Another key geographical consideration involves study area terrain. Many current dispersion models are based on empirical data that were collected in flat, open terrain, and are thus most applicable to these conditions. Several of the models do attempt to account for the effects of uneven terrain by considering differences between source and receptor ground-level elevations. The VALLEY model has been designated as applicable for screening analyses in complex terrain, although its treatment of plume impaction in complex terrain has been widely criticized, and thus its applicability must be considered limited. A more microscale land-use consideration that may be important in selecting a model is the presence of buildings or other obstacles adjacent to the source. The more refined UNAMAP models have limited capability to treat the wake effects created by such features.

Data Requirements: All models require information on the sources to be modeled and the meteorological conditions to be examined (Holzworth, 1972). For area sources, the models require a description of the size of the area and the emission rate. In many applications, source data can be obtained as emission factors from the "Compilation of Air Pollutant Emission Factors" (AP-42 as revised) (EPA, 1983b). For point sources (e.g., an incinerator stack), the models require the emission rate of one or more pollutants, the height of release, the diameter of the stack, the exit velocity of the gases, and the temperature of the gases as they are released. In some applications, a flow rate may be required instead of stack diameter and velocity; multiple point models require a location for each source. If downwash is considered, the dimensions of an associated building will be required.

Many routine applications use data from nearby locations, such as airports, National Weather Service stations, and military installations to represent the atmospheric conditions for the area of interest. The primary source for surface and upper air meteorological data is the National Climatic Center (Asheville, North Carolina). Long-term models use a climatological summary of atmospheric conditions, commonly referred to as a "STAR" deck. The STAR deck summarizes meteorological conditions in terms of joint frequency distributions of wind speed, stability class, and wind direction. This information has been developed for many locations in the United States and is also available from the National Climatic Center.

Averaging Period: Averaging period probably will be one of the major criteria used in model selection. The basic Gaussian equation calculates a short-term concentration representative of about 10 min to 1 hr. Hourly data are the basic calculation input for short-term models. The concentration estimates are often averaged for 3-, 8-, and 24-hr periods. Generally, it is also possible to use a full month, season, or year of hourly values to produce long-term estimates. As an inexpensive alternative, some of the models use an integrated form of the basic Gaussian equation and a statistical summary of the meteorological data (STAR tabulations) for rapid calculation of annual averages. These models are referred to as "long-term" or "climatological" models and are typically used to calculate 1-, 3-month, or annual averages.

5. Accuracy and limitations of air models: Three major factors influence the accuracy of air quality simulation models according to the American Meteorological Society (AMS, 1978, 1981). These are: (a) the capability of the algorithms to reproduce the important physical and chemical processes; (b) the quality of the emission data; and (c) the quality or appropriateness of the meteorological data. The overall accuracy of the Gaussian dispersion model will be dependent upon the specific application. The Gaussian model will perform best under the conditions used to form the basis for the current models. These conditions include: (a) low-level, continuous, nonbuoyant emissions, in simple terrain; (b) near neutral stability, steady and relatively homogeneous, and wind field; and (c) local, short-term, concentrations of inert pollutants.

Under these relatively simple conditions, "factor of two" agreement between predicted and observed concentrations is probably realistic. This estimate of accuracy assumes that the controlling meteorological parameters are measured on-site, an assumption that in many practical applications is not valid. At present, routine dispersion modeling applications often rely on ground-level observations taken hourly at NWS airport sites. These observations are intended primarily for aviation needs, and are not particularly well suited to dispersion problems.

Meteorological data requirements are substantial for diffusion modeling from point sources (AMS, 1980). With a complete range of meteorological measurements and correspondingly accurate emissions data, true concentrations for the simple dispersion case can probably be estimated to within ±40% (AMS, 1978). Complicating features in the specific application can substantially increase the uncertainties in the results. Such features include:

1. Aerodynamic wake flows of all kinds.
2. Buoyant fluid flows and accidental releases of heavy toxic gases.
3. Flows over surfaces markedly different from those represented in the basic experiments, e.g., forests, cities, water, rough terrain.
4. Dispersion in extremely stable and unstable conditions.
5. Dispersion at great downwind distances (> 10 to 20 km).

Significant improvements in dispersion modeling will require more direct observational knowledge of dispersion under these conditions. Model users should be aware that the capabilities of the current UNAMAP series to represent these features are based on a few special case studies.

Perhaps the most difficult situation to model with any accuracy would involve a low-level accidental release of pollutants. Here, uncertainties in the source emission rates probably would be the dominant factor determining accuracy of the concentration estimates. In this case, the time and space distribution of concentrations would be as important as overall concentration levels. Order of magnitude estimates of concentration within the area covered by the effluent may represent reasonable limits of accuracy for the hypothetically "perfect" model.

All of the preceding examples refer to short-term concentration estimates for point sources. No estimates of accuracy are available for cases where the basic point source model is extended (with modifications) to the prediction of dispersion from large area sources, or for long-term average dispersion. More confidence generally can be placed, however, in long-term predicted concentrations than in short-term predictions of worst case impacts (EPA, 1980). Khalil and Rasmussen (1985) have reviewed modeling of chemical transport and mass balances in the atmosphere.

E. Ecological Models

Ecological models for the transport, dispersion, accumulation, degradation, etc., of chemicals in environmental biomass are at a rudimentary stage of development compared to the single media physicochemical models discussed in preceding sections. Attempts to develop models for complicated biotic systems are a relatively recent endeavor (Travis, 1985), but Pritchard's extensive review of microcosm and model ecosystem studies cited over 200 references (Pritchard, 1982).

Ecological models can be classified in two categories according to the kind of simulation used (NAS/NRC, 1975):

Laboratory and field microcosm models - These are empirically based models developed by observations on systems of a small number of species of a small area under reasonably controlled physical, chemical, and biological conditions (e.g., bench-top systems, small ponds, and test plots).

Theoretical - These models usually are computer simulations of the time-dependent behavior of ecosystems and subsystems based on mathematical expression of assumed interrelationships and input data.

To a considerable extent, ecological models have focused on potential impacts on organisms rather than on the quantification of transport and fate processes.

Qualitative and semiquantitative ecosystem models have been described in the literature for several specific chemicals, such as persistent organics, heavy metals, and radionuclides (White and Burton, 1980; Travis, 1985). They focus primarily on food chains, particularly those leading from agricultural or industrial practices to yield serious exposures to humans or predator species at the top of the chain. Quantitative models tend to be applicable to specific chemicals in carefully defined systems. Mathematical pharmacokinetic expressions can describe uptake or decomposition rates (much as in chemical kinetics) for simple organisms or populations, but generally are not applicable to a complex environmental population. Models that routinely treat such processes as metabolism and biotic transfers across media generally are unavailable.

Data requirements for ecological models are substantial and can include uptake rates by organisms, metabolic reactions and rates, bioaccumulation (bioconcentration) or biomagnification rates, and interbiotic/intermedia transfer mechanisms and rates. For even a simple ecological model, all the data needed for a specific chemical may not be available, and estimation methods for missing data (e.g., use of structure-activity relationships) may be inadequate for quantitative modeling.

F. Intermedia and Multimedia Models

Most early research toward the development of transport and fate models for environmental contaminants used a single medium approach. More recently, a serious need has been recognized for models that could accommodate intermedia transfers of contaminants and that could yield multimedia exposure assessments. One approach to developing inter/multimedia models is to link selected existing single medium models in a way that reflects the sequential and parallel processes that actually occur in nature. The UTM, described under water runoff models, was one of the first such models (see below).

Multimedia models can be divided into two classes: screening and site-specific. The data needs for multimedia transport and exposure assessment models are extensive. Hedden (1982, 1984) has reviewed the data needs, which can include hydrologic and meteorologic data, site-specific media properties, and chemical-specific transfer parameters.

Screening models - These models are used when the data base on the chemical and its receiving environment are inadequate. The simplest of these are partitioning models that assume a pollutant is partitioned (usually at equilibrium) between environmental media; examples are ENPART, discussed below, and two models developed at Arthur D. Little (Lyman, 1981). A more complex model is TOX-SCREEN, also discussed below.

The Environmental Partitioning model, ENPART, uses fugacity equations to estimate ratios of chemical concentrations in air, water, and soil under equilibrium or dynamic (intermedia transport and transformation) conditions (Wood et al., 1982). The model provides a first-level screening analysis of a chemical and its partitioning in the environment. It is an interactive or batch model with the ability to receive a minimum set of input data for the physical chemical properties of a compound and calculate other properties required using correlations. It also has the ability to receive input of degradation and transfer rates or to supply default values. The interactive mode allows sensitivity analyses of various parameters of a substance to be performed quickly and easily.

TOXSCREEN is a screening level multimedia model, developed at Oak Ridge National Laboratory for the U.S. EPA, Office of Toxic Substances, to assess the potential fate of toxic chemicals released to air, surface water, or soil. The model is said to be simple in nature and is intended to be used as a screening device to identify chemicals that are unlikely to pose environmental problems even under conservative assumptions. It integrates SESOIL with other analytical models to provide a profile of chemical concentrations in multiple media surrounding a release site. It accounts for intermedia transfer by volatilization, disposition, runoff, and percolation (McDowell-Boyer and Hetrick, 1984). The program, written in FORTRAN for the DEC VAX 11/780 computer, is available on magnetic tape from the National Technical Information Service Computer Products (Kaufman and Kinerson, 1985b).

Site-specific models - These models include two versions of the UTM and GEMS which can be used in either screening or site-specific applications. The Unified Transport Model, UTM, is actually a group of models from which selected models are used in series, the output of one serving as the input of the next, to provide a multimedia model for a given study problem (Hedden, 1984). The UTM model requires data on temperature and dewpoint, hourly precipitation, daily wind speed, soil and vegetation characteristics, and watershed topography, in addition to data on the metal being modeled. The UTM model requires site-specific application. UTM was limited in its original version to trace metals (Munro, 1976), but has recently been modified (as UTM-TOX) to accommodate organics (Patterson et al., 1984). UTM-TOX is said to be capable of addressing pollutants from point and nonpoint sources, dispersion in different media, wet and dry deposition, surface and stream flows, soil erosion, and percolation through the soil to groundwaters or surface waters (Travis, 1985).

The Graphical Exposure Modeling System, GEMS, is a network of models assembled by EPA's Office of Toxic Substances for assessing potential human exposures to toxic substances from production of proposed new chemicals or from existing production. The system can integrate several data bases and models. GEMS can estimate, if necessary, the physical and environmental properties of a chemical from its structure-properties data base, and can utilize site-specific data on environmental characteristics to estimate transport and transformation rates. Models accessed through GEMS include: ATM and ISC for point and area air emission sources; BOXMOD for diffuse urban emissions to air; EXAMS for surface waters; SESOIL for the unsaturated soil zone; AT123D and SWIP for groundwater transport; and ENPART and TOXSCREEN for intermedia and multimedia phenomena. GEMS can utilize locational data for a release site and access 1980 U.S. Census Bureau population/demographic data to predict exposure concentrations and numbers of people exposed to air pollutants via ATM-SECPOP. GEMS also contains three subsystems for estimation of physicochemical properties (including bioconcentration factors) for chemicals: CHEMEST (development by A. D. Little Company), AUTOCHEM, and CLOGP3.

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VII. EXPOSURE PREDICTION

Exposure prediction involves using selected chemical and demographic information to estimate which and how many people (or other populations and values of concern) could come into contact with the environmental contaminants being studied and for what period of time. It combines information from the environmental transport and fate analysis on the concentrations of the contaminants with appropriate information from demographic and other population studies, and estimates the overlap of contaminants and populations in space and time. It requires concurrent consideration of where people live, work, and play, and of the routes, concentrations, frequencies, and durations of exposures to which they might be subjected.

A. Populations Potentially Exposed

Comprehensive assessments of the effects of environmental contaminants can require consideration of exposures of several kinds of populations and subpopulations. Populations can be considered conveniently in five generally distinct classes as follows:

- Workers at sites where contaminants originate or are being handled in large quantity.
- Members of the public whom the contaminant may reach.
- Natural populations of flora and fauna.
- Plants and animals of agricultural, commercial, and aesthetic value (e.g., crops, forests, fisheries, ornamentals).
- Other objects of economic or aesthetic value (e.g., corrodable paints, structural materials, and works of art).

The following discussion briefly addresses occupational exposures, but focuses on exposures of the general public. Resources did not permit further discussion of other kinds of exposures suggested above, but many of the principles noted under general population exposures also apply to them. In most decisions at EPA, exposures of humans to hazardous substances are likely to be the primary concern.

1. Occupational exposures: Workers at facilities where hazardous substances are present at high concentrations and in large quantities can be significantly exposed to such substances if proper safeguards are not maintained. Many studies have been made of occupational exposures at plants that produce, formulate, or use any of hundreds of commercial chemicals. Guidelines and regulations for worker exposures have been established by industry and government for many chemicals. For example, the National Institute of Occupational Safety and Health, several industrial firms or trade associations, and some unions have compiled data on typical exposures, based on analysis of air or materials in the work place or of body fluids of workers.

The American Conference of Governmental Industrial Hygienists, the Occupational Safety and Health Administration, and in some cases state or local agencies have published guidelines or standards.

Workers involved in treating, handling, transporting or disposing of hazardous wastes at TSDFs generally would be covered also by regulations on specific chemicals, although potential exposures may not be well documented, particularly when complex mixtures of chemicals are present. Workers involved in spill cleanup or corrective actions can also be exposed. Worker exposures tend to be site specific and are difficult to estimate quantitatively. They can vary with the chemical and physical nature of the materials being handled, the technology being used, and control measures and training programs in place. They can vary with the particular job or work station at a given facility and the individual's use of available control measures and prescribed practices (e.g., use of dust masks). The primary route of exposure is likely to be inhalation, but absorption through the skin, and hand-to-mouth transfers are also possible.

The assessment must identify the types of workers exposed, the number of each type, and the frequency, intensity and duration of exposure to all relevant toxicants. In addition, secondary exposures of worker's families can occur occasionally when toxicants are carried home on worker's clothing or bodies. While such exposures are probably small for workers in well-run modern manufacturing plants, this possibility should not be neglected in an assessment of hazardous waste disposal facilities.

2. General population exposures: Members of the general public can be exposed to hazardous substances in several ways. The present discussion will focus on exposures to contaminants moving through environmental routes and will not include exposures to chemicals used directly in the production of foods, medicines, or consumer products. Assessments of exposures to environmental contaminants must consider three factors: where people live; where they work; and other lifestyle factors that might increase exposures. Exposure routes that must be considered include inhalation of contaminated dusts, mists and vapors, ingestion of contaminated water, food, beverages or other substances, and dermal absorption following contact with contaminated substances.

In assessments involving hazardous wastes, attention usually will be directed to the TSDFs as potential point sources of contamination. In some cases attention must also be given to transportation accidents that would cause additional point (or possibly nonpoint) sources. In either case the environmental transport and fate studies or modeling runs will have provided information on the spread (both geographically and over time) of the pollutants from the source through the air, surface water, groundwaters, and other environmental compartments.

For air emissions, dispersion of the plume over residential areas would lead to inhalation of pollutants. Inhalation at site-specific commercial or institutional facilities may require consideration in some cases, and alternate exposure routes (such as deposition of pollutants on foods or surfaces) may require attention in others. For pollutants entering surface or groundwaters, contamination of water supplies could lead to ingestion of contaminants in drinking water and foods or beverages. Private wells, public water supplies, and both home and commercial food processing should be considered. For some pollutants absorption through the skin during bathing or other contact and inhalation of chemicals volatilizing in the shower may require consideration. In some cases lifestyle factors such as daily commuting through a dispersion plume or frequent recreational activities in potentially contaminated lakes or parks may need to be considered. A preliminary analysis of the geographical distribution and population distributions then determines the major exposure routes and populations that should be analyzed quantitatively.

Given the geographical boundaries of the pollutant's dispersion (coordinates of latitude and longitude) from the source site, a detailed population profile can be developed for the study area. The U.S. Bureau of the Census data provide one useful starting point, the most recent being the 1980 Census of the Population. In it, population enumerations are broken down by urban and rural areas, age, race, sex, commuting patterns, and household data. All data can be related to coordinates of latitude and longitude, but the level of specification will be less in rural than in urban areas (DOC, 1983). Because pollutants follow natural patterns rather than political and statistical boundaries, the Census enumerations will often have to be split to develop the population profile.

Several data bases besides that of the U.S. Census Bureau can correlate their data by latitudes and longitudes. Some models contain programs that access population data bases. For example, using GEMS, the ATM model is coupled with the Sector Population (SECPOP) program to retrieve 1980 population data. The model calculates the average annual concentration and exposed population for directional sectors radiating from the emission sources.

State agencies are another potentially valuable data source. Most state geology and land survey divisions work closely with the U.S. Geological Survey (USGS) and publish water supply and water resource information. Land usage information can be obtained from local governments or planning commissions. Local planning commissions may be able to provide current and projected community growth in the study area. Table VII-1 lists sources of certain specific data related to exposed populations.

Several U.S. government agencies and EPA divisions are currently trying to use the EPA's REACH File as the standard geographic coding mechanism for data storage. The EPA's Federal Reporting Data System (FRDS) lists ~ 60,000 community water systems of which ~ 80% obtain at least some of their water supply from groundwater. In some cases, on-line water treatment such as granular activated carbon is indicated; this would be a modifying factor in an exposure estimate. The USGS Groundwater Site Inventory file lists privately owned wells and springs.

TABLE VII-1

SPECIAL DATA SOURCES TO ASSIST IN PROFILING A POPULATION

Data Bases	Description of Information	Contact
Census	Demographic characteristics; includes commuting patterns and enumeration by school distict	U.S. Bureau of Census 301-763-7315
Drinking Water Supply File	Provides locations of water utilities, intakes, and sources	EPA 202-382-7046
Groundwater Site Inventory File	Lists locations of public and private wells and springs	USGS 703-860-6031
Inventory of Public Water Supply	Lists detailed information about 60,000 community water systems and 160,000 transient water systems	EPA 202-382-5551
REACH File	Lists the intersections of rivers with tributaries, lakes, and other water bodies	Monitoring Branch EPA 202-382-7074
STAR and Ground Conditions	Contains wind distribution (rose) data, dominant wind direction, precipitation and temperature	National Climate Center, NC NOAA 704-258-2850

Limitations on profiling the population effectively are: (a) the quality and completeness of the data available; and (b) the ability to specify pertinent subpopulations and to obtain geographically coded information. Extrapolated data from other areas may be useful, at times, in supplementing the development of the population profile. Daily human activity patterns and short-term population fluctuations such as commuting patterns, school hours, etc., may also need to be weighed, but are difficult to quantify confidently.

Since the intensity of health effects could be compounded for individuals in the general population who are unusually sensitive to the pollutant of concern, the presence of such individuals should be noted for consideration in the health impact analysis. Background health data, some of which is regionally and locally specific, are available through the National Center for Health Statistics, Center for Disease Control, and state and county health agencies.

B. Estimated Exposures

The estimation of exposures involves two phases: (a) development of exposure profiles for population groups; and (b) integration across population groups.

1. Exposure profile: An exposure profile must be developed for each of the identified exposed population groups. This profile should identify three characteristics of the exposure:

- Route of exposure: air, water, foods, soil, or other routes
- Time over which exposure will occur: time to onset and duration
- Concentration of contaminant received: concentration by route and variation over time

Average rates for intake of air, water, and food for humans are available (see Table VIII-2). Estimates of the intake of contaminated soil in different activities by children and adults have also been published (Hawley, 1985).

2. Exposure integration: The exposure integration process involves aggregating exposure to the extent possible over routes, concentrations, time, and population groups. The degree of aggregation that is reasonable can depend on several aspects of the contaminants. The toxicological properties of the chemicals of concern will be particularly important, but physical-chemical properties and route of exposure may also require consideration.

For example, if the chemical is nonvolatile and the health effect of primary concern is lung cancer after prolonged inhalation of it as a dust, then exposures via drinking water probably should not be routinely aggregated with those from air emissions to calculate the total exposure. Similarly, dermal exposures to a chemical that can be readily absorbed from water would be dissimilar to dermal exposures if it is tightly adsorbed on dust particles, and the two should not be routinely summed. The toxicological literature documents many examples in which the health effects differ depending on the dosage route. In other cases, however, response is similar for different dose routes. For long-term, low-level environmental doses to most chemicals, exposures by different routes usually are assumed to cause similar responses in the absence of information to the contrary.

Aggregation across population groups requires considerable care. In particular, if exposures vary widely across groups, the "most exposed" groups or individuals (MEIs) should be identified. They generally should not be aggregated with all other groups to calculate an average or mean exposure level. The reason is that most of the adverse health impacts could be incurred by a small number of highly or frequently exposed persons. The validity of this reasoning is most easily seen for a chemical with a well-defined threshold exposure level (i.e., only exposures above threshold cause adverse effects). It also holds true, however, for effects such as cancer that are assumed not to have threshold exposures, because the uncertainty range of estimated health effects usually increases rapidly as exposures decrease from those reported in toxicological or epidemiological studies used as reference points.

Aggregation across time also requires care in that some health effects are associated primarily with short-term exposures at relatively high concentrations, while others are associated with long-term (even lifetime) exposures at lower levels. Hence, population groups with substantially different temporal aspects of exposure should be treated separately in the health effects estimation and should not be aggregated in the exposure prediction.

In summary, the integrated exposure assessment tabulates all significant population groups according to the relevant environmental dose that each is estimated to receive.

References to Chapter VII

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VIII. HEALTH EFFECTS PREDICTION METHODS

Risk assessments involving toxic substances require predictions of the type and degree of adverse health effects that would likely result from given exposures. Such predictions require first a review of appropriate epidemiological, toxicological, biochemical, and other health-related literature for the chemicals involved in order to identify their effects on humans, other species, or other test systems under known conditions of exposure. They require, secondly, an evaluation of methods for extrapolating health effects from the known conditions to those of the problem at hand. The most appropriate predictive methods are then applied to the information from the literature to estimate the probable effects under expected conditions of environmental exposures.

This chapter characterizes the health effects data base typically available for chemicals of interest, and the models that have been proposed for health effects predictions. The discussion is broad, but not exhaustive. It is intended to give the reader an overview of the strengths and limitations of the field. Good recent reviews of most of the topics covered are available elsewhere, e.g., NAS/NRC (1975); OTA (1979, 1981); Richmond et al. (1981); CMA (1984); Clayson et al. (1985); Ricci (1985); Woodhead et al. (1985); OSTP (1985). It provides a basis for the general methodology described in Chapter X.

A. Characteristics of Health Effects Data

Virtually every chemical has the potential to produce adverse health effects in biological organisms if administered in sufficient quantity over a sufficient period. The nature and degree of toxic response depend on the chemical, the conditions of exposure (e.g., route, concentration, duration), and the nature and condition of the receptor organism. The literature contains information on many kinds of adverse health effects from a large number of chemicals under a wide range of study conditions, including different routes and temporal patterns of exposure, different degrees of control over exposure, and different test species or biological systems. A risk assessment of potential environmental exposure to a given chemical, ideally would use as a reference the results of one or more carefully controlled studies made under test conditions very similar to the environmental conditions. Practically, however, such ideal reference studies seldom are available, and the analyst must draw on a more extensive literature to predict potential adverse health impacts.

Several approaches are used in toxicity studies, depending on the properties of the chemical of interest, the health effect of concern, the type of information desired, and the resources of the researchers. For example, rapid effects of inhalation may be of primary concern for a new gaseous industrial chemical, while long-term effects of ingestion would need to be known for a food additive, and the mechanisms of DNA interaction might be of interest for a known mutagen. Since information developed by different approaches is complementary, information from one or more specific studies on a given chemical and the substantial body of background health effects information often will be needed for predictions.

1. Types of exposures: Exposure to a toxic substance occurs when the substance is present at the interface between a biological organism or test material and its environment, e.g., when the substance is in air we breathe, in food, water, or other liquids we ingest, or in materials we use or contact. Exposure subjects may be humans, laboratory and domestic animals, microorganisms, cellular preparations, or pertinent biochemical test systems. Exposures can be controlled and known, as is usually the case in pharmacological or toxicological studies with humans (e.g., of medicinal or consumer products) and in toxicological studies with nonhuman species and other biological component systems; or they might be uncontrolled or uncertain, as is the case of clinical reports or epidemiological studies of humans exposed to contaminants in the workplace or through foods or the environment.

In controlled studies, the substance may be administered in air, food, or water, by gavage (by tube into the stomach), by injection under the skin (subcutaneous), or into a body cavity (e.g., intraperitoneal). The administered dose is the amount of substance that actually contacts or enters the organism through bodily membranes or portals. The total administered dose in a study is a product of the concentration of the substance in its carrier, the volume of carrier crossing the interface per unit time, and the frequency or duration of dosage. In many cases, however, the total administered dose is not too useful a measure for making comparisons, and response will be reported as a function of simpler variables such as concentration mass or time. In other cases, particularly if the substance is rapidly excreted or metabolized by the organism, the concentration of the substance in the blood or at the affected organ site may be a more meaningful measure, and will be reported as the delivered dose or the effective dose.* The delivered or effective dose can vary depending on the route, carrier, and timing used for the administered dose, and also with the test species at a given dose. The concentration of toxicant at the site of action on a cellular level most often is not linearly related to the administered dose; a sigmoidal (S-shaped) relationship is common.

For environmental contaminants, the term environmental dose is analogous to the administered dose in controlled studies. (Unfortunately, the term "exposure" often is used also in a quantitative sense for environmental dose.) As in controlled studies, the effective environmental dose and hence the response, can depend on the conditions of exposure.

The temporal characteristics of exposure can have significant effect on the magnitude and even the type of response. For example, the effects of a large single dose of alcohol may be readily apparent (inebriation, and possibly death), whereas the same quantity administered over many days may have little effect. On the other hand, some substances administered frequently at levels without obvious effect may accumulate in certain organs and cause subsequent adverse effects. For humans both short-term and long- term exposures can be important.* The traditional series of toxicological studies with laboratory animals includes acute, subchronic and chronic exposures, and special studies which can address effects at certain developmental stages or in subsequent generations following exposure (see Animal Studies below for further discussion).

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* The term "effective dose" occasionally is used to mean "minimum dose causing the effect," which is more often called a threshold dose.

2. Types of effects: Toxic effects have both qualitative and quantitative aspects. An increase in the number and severity of effects can occur with increasing exposures; an increase in the prevalence of a given effect (or response) with dose can be of primary interest at times.

a. Effects of concern in risk assessment: All significant adverse human health effects (end points) should be considered in risk assessments. These include effects usually seen as a result of long-term (chronic) exposures, and those seen after shorter exposures. The health effects of concern include general toxicity: effects on digestive, respiratory, or cardiovascular systems; effects on central nervous system (neurotoxicity); effects on the liver (hepatotoxicity); effects on the kidney (renal or nephrotoxicity); and growth and development rates. Other health effects of concern will also include: oncogenicity (causes tumors of any kind), carcinogenicity (causes cancer or leukemia), mutagenicity (causes mutations), embryotoxicity or fetotoxicity, teratogenicity (causes deformed fetuses), induced sterility or decreased reproductive success, adverse behavioral effects, and cellular or subcellular effects. Table VIII-1 summarizes the range of effects of potential concern.

The literature will contain a variety of information and data, including observations and experimental results involving exposures of humans, animals, or other test organisms or substances, and conclusions regarding the range of adverse health-related effects. Different chemicals may produce different characteristic adverse effects, but a given chemical may also produce several different effects (one or more nonlethal effects and perhaps death) in different dosages and exposure situations. EPA has proposed guidelines for assessing the risks of carcinogens, mutagens, and developmental toxicants (Anderson et al. 1983; EPA 1986a, 1986b, amd 1986c). The literature can be inconclusive about whether a chemical causes a given effect, particularly cancer. The international agency for research on cancer established guidelines for evaluating evidence of carcinogenicity, and has reviewed available evidence for many chemicals and classes of chemicals in a series of reports (IARC, 1977).

b. Measures of response: Biological response data are reported in one of three ways: quantal, graded, and continuous.

Quantal (dichotomous) data are based on a "yes-no," "all-or-none" determination of a specified end point. A test subject has the effect

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* For example, both 15-min peak exposures and continuous, lower-level exposures may be addressed in setting workplace standards.

TABLE VIII-1

ADVERSE HEALTH EFFECTS THAT CAN BE CAUSED BY EXPOSURE TO SOME CHEMICALS

Debilitating Effects

- Allergies
- Asthma
- Arthritis
- Behavioral disorders
- Cirrhosis
- Dermatological disorders
- Emphysema
- Endocrinological disorders
- Immunological disorders
- Neurological disorders
- Renal disorders
- Severe weight loss

Reproductive and Genetic Effects

- Sterility or decreased fertility
- Miscarriages and spontaneous abortions
- Reduced weight or vigor at birth
- Teratogenic effects
- Mutagenic effects

Frequently Fatal Effects

- Cancer and leukemias
- Central nervous system disorders
- Severe respiratory or gastrointestinal distress
- Heart and circulatory disease
- Liver function loss

or it does not. Data are reported, for example, as percent of subjects dead, percent with cancer, or percent with skin irritation. Quantal data are used extensively for toxicological comparisons, particularly as indices of potency. Best known of these is the lethality index, the LD_{50}, which is the quantity of substance which kills one half of the test subjects (i.e., the median dose). The LD_{50} is usually stated as milligrams of substance per kilogram of body weight of subject (mg/kg) but can be in other units. The LD_{50} is usually one of the first toxicological parameters determined for a chemical, but its value often varies with the species, strain, and the sex of the test animals, and between laboratories. Oral LD_{50}'s are usually lower than dermal LD_{50}'s, but higher than intraperitoneal LD_{50}'s. The LD_{50} is one of the most reproducible of toxicological parameters, but a two-fold variation between species (or at times between test groups of the same species) is not uncommon. For some purposes, knowledge of other toxic dose levels may be desirable, such as the LD_{10} or TD_{50} (causing 50% tumorigenic response above background dose). Quantal data are used in most of the common risk extrapolation models.

Graded data are based on a step response concept of severity of the response, e.g., absent, minor, moderate, severe, very severe. The graded format is not used extensively to report toxicological data (pathological reports on lesions are one exception). Graded data are considered to be a subset of quantal data by some authorities (Klaassen and Doull, 1980). In quantitative risk assessment, graded data usually would be transformed into quantal data for use in extrapolation models.

Continuous data are often based on the degree of response within individual test subjects, as well as among individuals. Typical data in the continuous response format might include: percent loss of weight; changes in performance or behavior; percent cholinesterase inhibition or carboxyhemoglobin in the blood; or percent reduction in respiratory function or sperm levels. Although such end points can be quantitative, they are not necessarily direct measures of toxicity, or may not reflect basic toxicity mechanisms.

3. Types of dose-response relationships: If exposure to a substance causes a given adverse effect, then the relationship between the dose and the measured response will usually take one of a few familiar patterns. A graphical presentation of quantal data usually will show a nearly linear relationship between response and dose (or logarithm of dose) in the midrange of the plot.* If data are taken at sufficiently low doses, the line usually is found to have convex curvature.** The upper portion also may be oppositely curved to give a slightly sigmoid (s-shaped) curve (the typical integrated normal distribution curve) as shown in Figure VIII-1A. Two good midrange data

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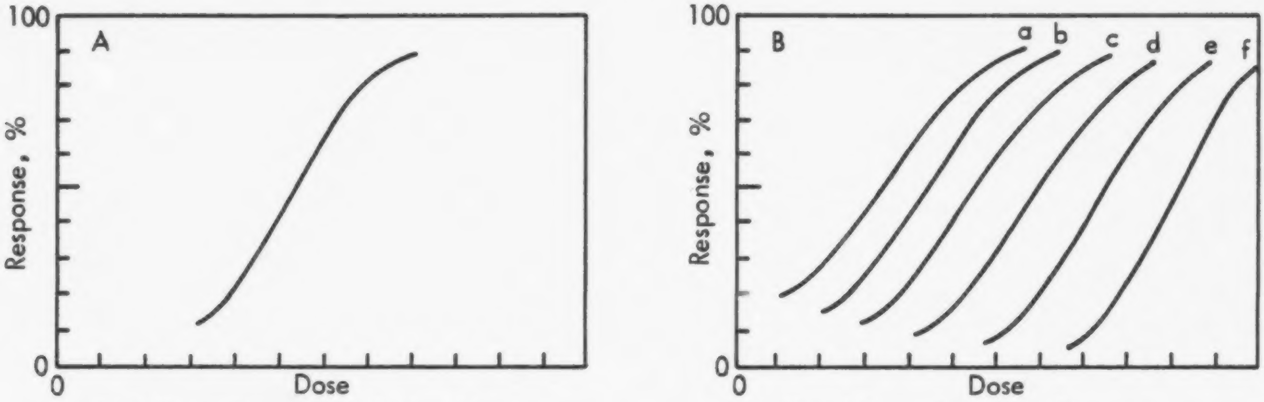
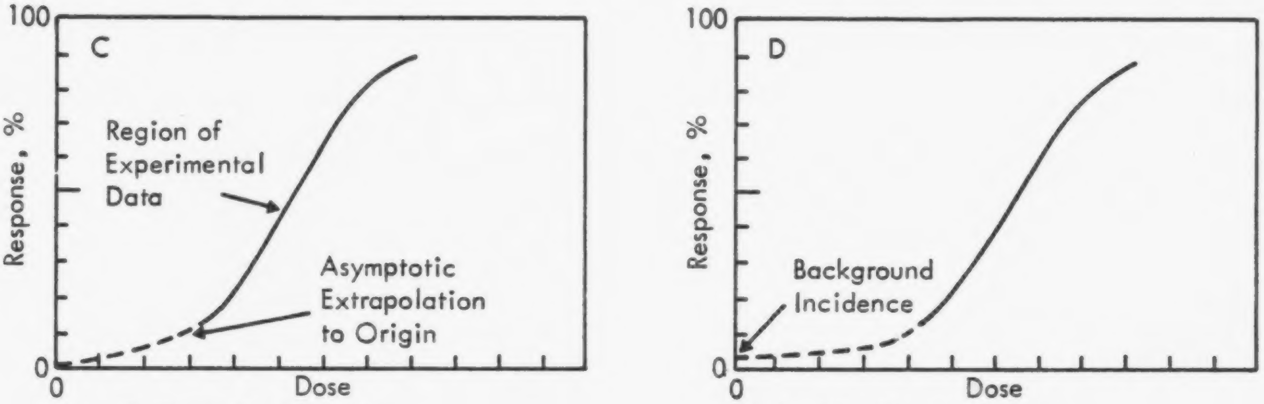
* Dose-respondent data are sometimes specified as dose-incidence for quantal data and dose-effect for graded or continuous data.

** Convex curvature often is called upward or sublinear curvature and concave curvature called downward or supralinear (OTA, 1981; Bickis and Krewski, 1985). One can find, however, an extrapolation to very low (or high) doses that exhibits concave curvature described as sublinear (NRC/NAS, 1983), and even the combination term "concave upward" (NRC/NAS, 1975).



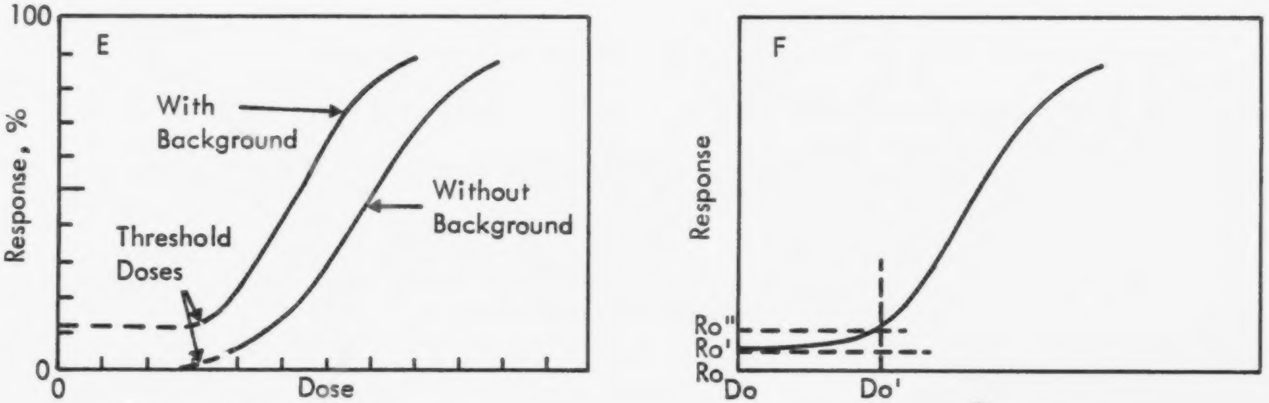
Typical Dose-Response Relationship Observed for Many Effects

Family of Dose-Response Curves for Multiple Effects of a Chemical



Smooth Curve Extrapolation to Low Dose

Typical Background Effect



Typical Threshold Effects

Transformation of Curve Shape with Background and Threshold Levels

Figure VIII-1 - Representative Dose-Response Relationships for Health Effects of Chemicals

Source: Midwest Research Institute

points (i.e., between about 16 and 84% response) are usually adequate for estimating an LD_{50}. The appearance of a given plot of data will depend on the dosage scale used and also on factors specific to the test, such as presence of a threshold or background, as will be discussed below. An essentially linear relationship passing through the origin is one possibility.

In general, exposure to a chemical will cause not just one but several types of response as the exposure level is increased. A family of dose-response curves could be developed, as shown graphically in Figure VIII-1B. At low doses, the response might be beneficial (in the case of a medicinal or essential nutrient) or relatively benign (e.g., subtle biochemical or physiological changes). At increasing doses, however, increasingly adverse responses may be revealed, e.g., various physical and behavioral symptoms; effects generally seen with chronic exposures, such as liver damage, cancer, or mutational effects; reproductive and teratogenic effects; and ultimately effects seen following acute exposures such as rapid debilitation or death. Data for such effects might be observed by a variety of approaches, including epidemiological as well as toxicological. The most immediate adverse effects should certainly be addressed in a comprehensive risk assessment, but longer term or less severe effects which may occur at lower exposures (particularly below the apparent threshold or threshold of concern for the most immediate adverse effects) must also be considered; some could be the effects of primary concern for exposures through environmental routes.

Several factors make difficult the extrapolation of the dose-response relations from the relatively high doses typically seen in toxicological studies of animals or epidemiological studies of workers to the low environmental doses of interest. These include experimental difficulties at very low dose (which make data points scarce and subject to increased uncertainty and scatter), and also the curvature that commonly occurs in the relationship in this region.* Assuming that the response is zero at zero dose, a straight line might be fitted to all the data points so that it also passes through the origin, or a straight line might be drawn from the lowest dose data point to the origin. Both have been used when the data are of minimal quantity or quality. If data are satisfactory, one might expect that the relationship could be extrapolated by inspection in a smooth, perhaps asymptotic curve to the origin, as shown in Figure VIII-1C.**

In many studies, the low dose responses do approach the baseline in this nearly asymptotic fashion. Such simple extrapolation has three weaknesses, however, that require caution before it can be applied in quantitative risk assessment of environmental exposures to chemicals: (a) sensitivity to dose; (b) background effects; and (c) threshold effects. In addition, temporal effects can influence the nature of the observed dose-response relationship. Each of these effects is discussed briefly below and then illustrated by the results of a major study of a carcinogen, the ED_{01} study.

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* Similar curvatures at the low end are known in the cause-effect relationships for many physical phenomena also (e.g., nuclear radiation, molecular ionization, chemical reactions); curvature can reflect a quantum mechanical "tunneling effect," as well as population variability and multifaceted causes of the effect. Curvature at the upper end can reflect the presence of highly tolerant members of the population or complications by other kinds of response (e.g., cells or organisms may be killed).

** The response at low dose is not necessarily normally distributed.

- Sensitivity of risk to dose: In cases where the asymptotic low dose relationship holds, the response (risk) changes too rapidly from about 1% or 10^{-2} to 10^{-10} over a small dose range to permit quantitative estimation at a given low dose with confidence. Mathematical expressions that fit the experimental data have been proposed for such extrapolations, but they also have weaknesses, as will be discussed in Section VIII.B.

- Background effect: In many cases the simple extrapolation shown in Figure VIII-1C also does not hold because a background incidence for the response exists in the study population, i.e., the curve intercepts the vertical response above zero, as shown in Figure VIII-1C. Experimental data for unexposed control subjects can demonstrate the presence of background incidence, although they do not demonstrate the complete absence of a small background. When a background level exists, it often increases with the age of the subjects. From a risk assessment and management viewpoint, the presence of a background incidence poses no conceptual problem, since it is the increase in response above background that is of interest, i.e., the background is subtracted out of the data. Practically, however, high background incidence for a given response in either the study population (particularly nonhuman subjects) or the potentially exposed human population will substantially increase the uncertainty in estimates of increased risk at low dose. In addition, mathematical extrapolations to low dose can depend on whether the background is considered to be independent of or additive to the response of the test substance.

- Threshold effect: In many cases the relationship apparently does not hold because a minimum or threshold dose is required to elicit any response or a response above background, i.e., the response to the chemical below the threshold is apparently zero, as shown in Figure VIII-1E. The highest dose (level) used in a test that elicits no observable effect (or no observable adverse effect) is called the NOEL (or NOAEL), and can be either slightly above or well below a true threshold that might be established by more extensive testing.

Thresholds are widely observed in biological response in individuals to many stimuli (e.g., taste, odor, light, heat, pain, etc.), and threshold-like relationships are typically found in pharmacological, toxicological and epidemiological studies also. A reasonably sound biological rationale often explains why a threshold could exist. For example, as noted in Section A.1, the delivered dose often holds a sigmoidal relationship to the administered dose, with a threshold effect, in some cases because of simple adsorption/clearance mechanisms. In addition, a detoxification or repair mechanism that is effective at low dose may become saturated and ineffective at higher doses. Conversely, biological rationales have been proposed that would preclude thresholds for cancer and some other responses.* Experimentally, the existence of a threshold can be neither proved nor disproved in toxicological studies of populations with a distribution of a given response. The number of test animals needed to acquire each significant new data point simply becomes too large at decreasingly low doses (e.g., thousands or tens of thousands of animals) to determine if a few very sensitive individuals exist. Whether or not a true threshold exists in a heterogeneous population for a given effect is a matter of faith based on the rationale used.**

Belief that thresholds should not exist for carcinogens became embedded in the so-called Delaney Clause of the 1958 Amendments to the Food, Drug and Cosmetics Act. Recently, reconsideration of the range of biological origins of cancer have led to suggestions that while threshold doses might not exist for some carcinogens, thresholds might exist for others, in particular, those associated with bladder or thyroid tumors. Carcinogens that act through "epigenetic" mechanisms (e.g., via formation of bladder stones) were viewed in one study as more likely to have thresholds than those causing somatic mutations (genotoxic mechanisms), although the data were not conclusive (OTA, 1981). In 1985, however, an expert review (OSTP, 1985) noted that a chemical that only causes cancer secondarily to a gross physiological effect is likely to have a threshold at some dose level below that which causes the physiological effect.

From a risk management viewpoint, belief that a threshold dose exists for a given chemical greatly simplifies regulation: the threshold is divided by a safety factor (e.g., 10, 100, or 1,000) that reflects the confidence one has in the data base and the quotient is set as the standard of acceptable exposure. Thus occupational exposures to a great many chemicals are regulated under threshold limit values (TLVs) (ACGIH, 1980, 1983). Levels of many chemicals in food products are regulated under the concept of acceptable daily intake (ADI), introduced by the U.S. Food and Drug Administration in 1954 using a 100-fold margin of safety (Lehman and Fitzhugh, 1954). With few exceptions, regulation of noncarcinogenic chemicals to date have been based on risk assessment that assume thresholds existed, whereas regulation of carcinogens has not (Moreau and Anderson, 1980).***

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* Even if the biological rationale precludes belief in a threshold dose for response, a threshold of regulatory concern can exist, and lead to the setting of a "virtually safe dose" (VSD) or tolerance level, e.g., aflatoxin in natural foods. VSDs obtained by mathematical extrapolation models can be as little as one millionth of the no (or lowest) observed effect level in a study.

** Brown (1976) discussed the mathematical aspects of the threshold concept in dose-response studies of carcinogens. Weinberg (1983) has noted the trans-scientific nature of regulating under conditions "beyond demonstrable effect."

***Risk assessments for regulating carcinogens have usually involved extrapolations to very low dose on a nonintercept log-log scale, as discussed in Subsection VI.B.2.

From a risk assessment viewpoint, belief in a threshold dose simplifies the analysis at doses clearly below threshold (i.e., the risk is assumed to be zero), but it does not eliminate the sensitivity problem cited above for simple extrapolation to the origin. Since thresholds are usually determined by extrapolation from low dose data with substantial uncertainty, the threshold dose itself is uncertain. Slightly above threshold, the asymptotic nature of the curve makes response relatively insensitive to dose, and risk prediction difficult at a given dose. At the threshold, the risk changes rapidly over a small dose from about 10^{-2} to 10^{-10}. In addition, thresholds can vary substantially between species and also between individuals, depending on their genetic makeup and their general health at times of exposure. Thresholds could be sensitive to synergistic effects. These factors all increase the uncertainty in estimating risk when environmental doses are in the threshold region.

As indicated above, both a background incidence and a threshold effect for increase above background could be observed in the same data. In practice, a threshold may be eliminated if the toxic mechanism of the test substance is similar to that causing the background, or a threshold may be revealed only if studies are made on populations with negligible background incidence. In essence, the basic shape of the curve is fairly constant, but the background and threshold levels of the particular chemical and population determines the low-end cutoff point and thus determines how much of the low-end tail is observable (see Figure VIII-1F).

- Temporal effects: Three kinds of temporal effects can influence the results observed in a toxicity study. The first is that some responses occur to a significant extent only after nearly continuous long-term exposures. Such responses may be missed in shorter studies, and possibly even in chronic studies at doses so high that the subjects die early of other effects. Results of good chronic studies (see subsection 4) are essential for risk assessment. The second effect involves latent response. Some effects, notably cancer, can occur long after exposure has occurred or even ceased. Latency periods of 10 to 25 years or even longer have been suggested for some human carcinogens. Hence, results of good chronic studies are again critical in assessing risks. However, the observed slope of the curve, background incidence, and minimum effect levels, can vary with the study period.* The third effect involves heritable genetic change in the exposed population, i.e., mutagenic effects. Studies of at least two generations following exposure are usually needed to assess mammalian mutagenic risks confidently. The effects on subsequent generations are generally a fraction of the effect for the first generation.

- Illustrative data: The ED_{01} study is the largest ever made of a carcinogen. The chemical was 2-acetylaminofluorene (2-AAF), a potent bladder and liver carcinogen. Over 24,000 mice allocated to 81 different treatment groups were dosed in feed at seven exposure levels (30 to 150 ppm plus an undosed control) of 2-AAF until sacrificed and examined. Groups were sacrificed at either 18, 24, or 33 months. Subgroups of mice were dosed only 9, 12, or 15 months and then sacrificed at either 18 or 24 months. The study was designed to estimate precisely the effective dose (sic) producing a 1% tumor rate in the mice (hence, the name ED_{01}). The study, its results, and analysis were published in a collected series of papers (Staffa and Mehlman, 1980), and in other publications.

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* Incidence of some naturally occurring cancers is reported to increase at approximately the 4th power of age.

Illustrative results from the ED_{01} study (Littlefield et al., 1980) are shown in Figure VIII-2A and VIII-2B for bladder and liver neoplasms. In brief, the bladder cancer results showed essentially no background, an increasing incidence with dose and exposure period (age at sacrifice), and a clear minimum observed effect level of about 45 ppm. The authors say, however, that the total results are consistent with a "no-threshold concept" of cancer. The liver cancer data, in contrast, showed greater variation. At 18-month exposures, background was negligible, and incidence increased slowly with dose; but at 24- or 33-month exposures, the background and the incidence rates increased dramatically. The 33-month exposure data illustrate the uncertainties in chronic studies at low dose with high background response: the scatter in the 30-, 35-, and 45-ppm dose data points occurred even though over 40 mice were in each group. (The composite data points were used to fit the curve in this figure.) The 24- and 33-month exposure data again suggest the presence of a minimum effect level of perhaps 10 ppm, although the authors stated the data were nearly linear and extrapolated directly to zero.* In the summary of the ED_{01} study Gaylor (1980) insisted that the data for bladder tumors did not support a threshold concept, those for liver tumors dispelled it, and together showed the impossibility of ever showing thresholds by animal studies. (Other conclusions might be drawn.)

The discontinued feeding studies also provided data important for assessing risks from carcinogens. Again, the results were different for the two kinds of cancer. Bladder neoplasm incidence was not as high in later life if dosing was stopped in midlife. The authors concluded that induction of these tumors appeared to be continuous across the lifespan of the mouse. In contrast, liver neoplasm incidence was 60 to 70% as high in later life if dosing was stopped in midlife as if it had continued. The authors concluded that these tumors were largely induced in early life. but not expressed clearly until much later.

Overall, the results of the extensive ED_{01} study suggest some of the kinds of uncertainties one should expect even in well performed toxicological or epidemiological research. The development of dose-response relationships for use in risk assessment require careful evaluation of all relevant data for a given chemical.

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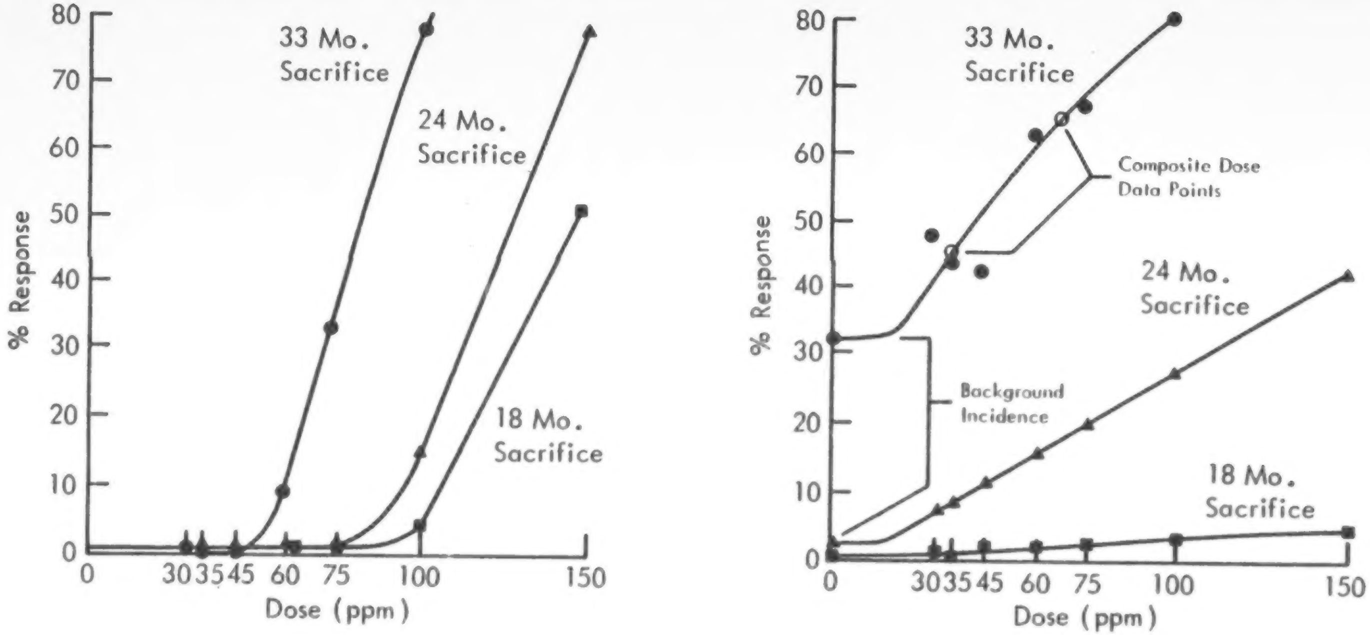
* The original graph (p. 27 of Littlefield et al., 1980) was inaccurately drawn and showed more linearity at low dose than actually existed (Figure VIII-2B). When data from sacrificed and dead/moribund animals were combined, the curves were changed slightly from those shown (Farmer et al., 1980).



A - Bladder Neoplasms

B - Liver Neoplasms

Source: Adapted by MRI from data on the ED_{01} study in Littlefield et al. (1980) (curves fitted by inspection).

VIII-2 - Dose-Response Data for Carcinogenic Effects of 2-Acetylaminofluorene in Mice

4. Data sources and quality: The data needed for a health risk analysis will depend on the specific nature of the chemicals present, the type of adverse responses they cause, and the nature of the exposure conditions. One would like to have descriptive information and quantitative dose-response data on the range of health effects in humans of the subject chemicals under controlled conditions closely approximating those predicted to occur. In practice, however, one rarely has such information, and must resort to alternative approaches based on the data that are available and the methods or models for using such data in health-effects estimation. Animal studies are usually an acceptable first alternative for toxicity data. If adequate data are available from neither human studies nor animal studies, one must look for other, less desirable alternatives. Each of these three kinds of data sources is described briefly below.

a. Human studies: Determination of risk factors for many kinds of technologically related threats is greatly aided if health-effects information on humans is available. Data on humans are obtained by three approaches: direct experiment, clinical observation, and epidemiological studies.

- Human experimentation: The use of human subjects in controlled studies is limited by ethical considerations to tests in which one can be confident that no serious or irreversible effects will occur. For example, human subjects could not be used to test the potential carcinogenicity of a substance. A substantial number of situations do require human-subject testing after other tests have demonstrated the general safety of the procedures (e.g., pharmaceutical testing, biomedical engineering applications, and the National Aeronautics and Space Administration manned space programs). These are controlled clinical studies which include laboratory analyses of physiological endpoints. Experimental laboratory studies on humans are more likely to be for less toxic substances or lower exposure levels; they usually address less severe effects such as skin, eye or bronchial irritation, and organoleptic effects.

Data from human experiments may be used in risk assessment similarly to data from animal toxicology experiments. However, human experiments generally provide "No Observed Adverse Effect Levels" (NOAELs), "Lowest Observed Adverse Effect Levels" (LOAELs), or "Frank Effect Levels" (FELs), rather than full dose-response data. The major limitation in trying to use human experimentation data in health risk analysis of hazardous waste is that few of the chemicals of interest have been tested in a controlled relevant manner.

- Clinical case reports: In addition to controlled experiments with human subjects, much useful information for determining human risks is developed through clinical investigation and observation of persons who have been unintentionally--and often excessively--exposed to a health hazard. An analysis of case reports on such observations can yield useful qualitative information, such as identification of endpoints at high exposures. The limitations of these data, however, are that exposures were uncontrolled, usually unknown, and seldom of the long-term, low level nature that are of most concern with hazardous wastes. When animal studies exist, clinical case reports provide verification of the adverse endpoint in humans. Reports of a series of cases, often found in medical journals, provide stronger qualitative support of the type and degree of adverse effect, but again usually no quantitative information. Occasionally, the number and quality of case reports may be sufficient to make feasible an epidemiology study (as described below).

- Epidemiological studies: Epidemiological studies seek to determine the incidence, distribution, and causes of injury and disease in humans. Epidemiology focuses on groups of people (rather than on individuals), and increasingly uses sophisticated biostatistical techniques. Epidemiological studies may have either a descriptive or an analytical orientation (i.e., focusing on either the distribution of a disease in a defined population or on the various factors associated with its incidence).

Descriptive (sometimes called ecologic) studies usually rely on an analysis of vital statistics. Vital statistics consist of rates of morbidity, mortality, incidence of diseases such as cancer or birth defects, and age and residential distributions. They are used to examine geographical variations and time trends of health effects in order to identify unusual kinds or areas of incidency, and if possible to compare them with concomitant exposure variations.

Analytical epidemiological studies provide measures of increased risk in the form of incidence or prevalence rates (Fisher, 1982). Analytical epidemiology has two* basic approaches: case control (often called retrospective), and cohort (often called prospective). Case control studies involve a group of persons who have a given disease and a control group of persons who do not have it; comparisons by age, sex, genetic composition, occupation, place of residence, life style, chemical exposures, etc., may reveal risk-related information for that disease. Cohort studies involve following the medical histories as they develop over several years of two previously identified groups, one of which has been exposed to the potential disease-related agent and one (the control group) which has not. Both approaches have strengths and limitations, but the cohort studies are usually preferred for estimating the health effects of exposure to a specific chemical. Day (1985) and Kraybill (1985) have reviewed the application of epidemiological methods to carcinogens.

Several aspects of experimental design must be evaluated to determine whether an epidemiology study is suitable for risk assessment. This includes examination of procedures used (a) to select and classify subjects, (b) to estimate their exposures, and (c) to follow their health effects. Other issues to be evaluated include control for potential confounding factors** and the selection of an appropriate control group. The measure used to summarize the degree of association between exposure and adverse effect is the ratio of the rate in the exposed population to the rate in the unexposed population. This rate ratio can consist of incidence or prevalence rates (relative risk), adjusted mortality rates (e.g., Standardized Mortality Ratio), or the rate of exposure in cases relative to that of controls (odds ratio). A ratio of unity suggests no association between the exposure and the effects. When the ratios do show an effect from exposure, the incidence rates from the study are suitable for use in quantitative risk assessment. Prevalence or mortality rates can be transformed to incidence rates when necessary.

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* Cross-sectional studies (also called prevalence studies) are sometimes considered as a separate approach. They measure the presence or absence of a disease and other variables at a fixed point in time.

** See for example discussions by Holland et al. (1979) and Bolten et al. (1983).

Epidemiological studies have several inherent limitations. One is that increases of commonly occurring health effects (such as cancer of the lung or colon) usually are not detected unless the change is very great. Another limitation is that exposures were not controlled, and are usually poorly known. In fact, many of the human data are obtained from industrial occupational studies in which sample size is limited by the number exposed, and exposure levels are determined by the circumstances of the industrial setting. Because of these limitations, a study may yield only a single or a few risk ratios that provide an isolated effect level. Such data do not yield a dose-response curve, and probably do not indicate how far the effect level is above the threshold level, if any. A further inherent limitation of epidemiology studies is that they may fail to reveal a true adverse effect due to insufficient data for some reason. When the data collection procedures and analysis are judged to be adequate, the determination of the validity of a negative study is largely statistical. Guidelines exist for distinguishing between valid and equivocal negative studies and for using isolated effect levels. Finally epidemiological studies may establish correlations, but may not be able to demonstrate a cause and effect relationship.

Despite these limitations, epidemiological results can be useful in quantitative risk assessment. Results of a conclusive epidemiology study are likely to be the best data available. Even if the results of an epidemiological study do not provide a dose-response relationship or are not conclusive in demonstrating the risk or absence of risk posed by a given agent, they can complement the results of other studies (e.g., animal toxicological tests, clinical case reports, actuarial analysis) and may be the deciding factor (particularly if they confirm other evidence) in reaching a regulatory decision for potential sources of a disease. See for example the review by Crouch and Wilson (1979) and specific studies on ethylene dibromide (Ramsey et al., 1978) and vinyl chloride (Gehring et al., 1979). Hattis (1986) suggests that "molecular epidemiology techniques"--combinations of analytical epidemiology with advanced biochemical methods--hold promise for quantitative assessment of a broad spectrum of human health risks.

b. Animal studies: The traditional series of toxicological studies with laboratory animals classified by length of exposure consists of acute (sometimes called single dose) studies, subchronic (sometimes called repeated dose, subacute, or short-term,* studies), chronic (often called long-term studies), and special studies (Doull et al, 1980).

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* Unfortunately, the microbiological and biochemical in vitro tests developed in recent years are also often called short-term studies.

Acute studies usually involve a single dose or, for inhalation, a single exposure of up to 24 hr. These studies use relatively high doses. Effects addressed in acute studies include death, irritation, and other relatively gross consequences. Acute toxicity has traditionally been about the first toxicological property to be studied for a chemical, and the LD_{50} is usually reported in the literature for studied compounds.

Subchronic studies range from those using a few repeated doses over a few days to those lasting 90 days (or about 10% of the subject's lifetime). Subchronic studies usually look for more subtle effects than do acute studies, such as changes in clinical chemistry values and microscopic tissue pathology, rather than lethality. Subchronic studies can yield quantitative dose-response relationships, but often are used to determine the range of appropriate exposures for chronic studies.

Chronic studies involve repeated and prolonged dosing for periods approaching lifetime (typically 2 years in rodents and 7 years in dogs). Chronic studies detect effects that are cumulative or have a latency period, and effects of bioaccumulated toxicants. The end points of chronic studies can be nominally the same as those of acute studies, but very often are different. Multiple dose levels are used; a study should identify target organs and tissues, the range of effects, dose levels where given effects are not observed and first observed, and the frequency and severity at increasing dose.

Ehling (1988) recently discussed the quantification of genetic risk of environmental mutagens, including the "direct," doubling dose and genetic number methods for Mendelian mutants, chromosome aberration methods, and methods for irregularly inherited disorders.

Special studies are designed to look at particular endpoints, metabolic systems or unusual situations. The most common are teratogenesis studies (looking for malformed fetuses) and reproductive studies (looking at fetotoxicity, reproduction and survival rates, and other developmental effects). Effects may be monitored for a lifetime, or in the second and third generation following exposure.

In toxicological studies, an effect will not be observed unless there is a receptive subject (e.g., pregnant female for teratogenesis*) and the effect is systematically sought (e.g., appropriate exposure period for carcinogenesis). One can demonstrate a specific adverse effect, but it is not possible to demonstrate the complete absence of adverse effects (i.e., establish complete safety), since true effects may not have been observed in statistically or biologically significant numbers, or may have been overlooked.

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* Teratogenic effects occur only when the female is exposed to the teratogen during a critical period during the gestation period--usually only a few days to a few weeks, depending on the species and the effect. The critical period is usually early in the gestation (first trimester for humans).

An adequate set of experimental animal data will consist of one or two reliable studies each of acute, subchronic, and chronic quantified exposures to the chemical in an appropriate dosing mode (e.g., by inhalation for air exposure, or by gavage, in feed, or in water for ingestion. A toxic response will have been studied at a minimum of three dose levels plus a control group. Ideally, the lowest dose tested will have negligible effects, one or more doses will have definite toxicity but no lethality, and one or more high doses will produce the substance's full array of toxic effects including substantial lethality. It is helpful if the total data base for the chemical also includes evidence that the effects would occur in humans. Inadequate animal data sets may still be useful, as discussed below, but will usually lead to risk estimates of lower confidence. Again, the ideal would be a reliable set of dose-response data for each kind of effect over the exposure range of interest.

- Limitations: The use of animal studies to predict human health effects has several inherent and practical limitations.

The inherent limitations include:

- Extrapolations, when required, across dissimilar exposure conditions, e.g., from uniform chronic exposure studies in animals to the short-term (even single dose) or intermittent environmental exposures often incurred by humans, or from subchronic animal data to chronic (even lifetime) human exposures. Such differences pose especially serious methodological problems when exposure to carcinogens is involved.
- Extrapolations from high doses used in animal studies to the low doses often encountered in human environmental exposures.
- Extrapolations across species of different sizes, metabolisms and habits. Different species often respond similarly to equivalent doses of a given chemical, but in many cases they do not. In some cases the mouse is not even a good predictor of response for the rat.
- Extrapolations across routes of exposure from animal studies to human environmental exposures.

The practical limitations include confounding factors, dosage accuracy, and negative results.

- Confounding factors include environmental factors (such as irregularities in lighting and air circulation, cleanliness of cages, and concomitant disease outbreaks), contamination or misidentification of the test chemical, and other accidents in the study which, in effect, change the terms of the experiment (e.g., a sick animal seldom reacts in the same way to a dose as a normal animal).

- Accurate knowledge of the dosage used for each test is extremely important, but is often difficult to achieve. The actual dosage delivered to an animal may not necessarily be the intended dosage, especially in inhalation studies of nongases but also in other tests with the toxicant dispersed in feed, water, or air. For example, some test material may decompose or be otherwise lost during the study. Equally important, at times the absorbed dose may be significantly less than the exposure dose.

- Negative data (no adverse effects observed) are not without uncertainty; a particular adverse effect may be statistically unobserved under the test conditions, or if it was not looked for, it was not likely to be reported, even if present. This is especially true for effects requiring special tests for detection, such as clinical chemistry or histopathology.

c. Other sources: If adequate data are unavailable from either human or animal studies, other data sources may still provide useful information for risk assessment.

Such information could include toxicokinetic data on the chemicals, toxicological data for humans or animals on related kinds of chemicals (cognates), or data on the chemical of concern from one of the variety of large *in vitro* bioassay studies* that have been developed over the last two dozen years. These are short-term tests that use microorganisms, cell cultures or biochemical systems; they provide information about a chemical's effects, particularly mutagenesis and, by extrapolation, carcinogenesis. The dose-response functions provided by these tests are difficult to extrapolate to effects in mammals. Such studies are widely used in prioritizing chemicals for chronic testing, but have not been accepted as a general substitute for mammalian studies. The potential use of studies of these kinds is discussed further under Section B, "Predictive Models."

d. Judging evidence of carcinogenicity: Carcinogenesis is an effect of particular importance, but studies of a given chemical often report different results depending on the species, sex, and exposure conditions. The International Agency for Research on Cancer has developed a weight-of-evidence system for judging information on a chemical's carcinogenicity (IARC, 1982). Evidence from both human and animal studies was characterized as either sufficient, limited, or inadequate, and the chemical was classified overall in one of five categories:

1. Sufficient evidence--Malignant tumors (a) in multiple species or strains, (b) in multiple experiments; (c) to an unusual degree regarding incidence, site, or type.

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* Literally "in glass" tests.

2. Limited evidence--Suggestive data (a) from a single species, strain, or experiment; (b) from studies with limitations in testing procedures; and (c) based on neoplasms that tend to occur often spontaneously or are hard to classify as malignant.

3. Inadequate evidence--Reported studies have major limitations that preclude confident interpretations.

4. Negative evidence--Studies report that within limits of tests used the chemical is not a carcinogen.

5. No data--No studies of the chemical are available.

EPA proposed slight modification of the IARC characterization scheme, and developed five overall classifications that can be summarized as:

> Group A - Human Carcinogen - sufficient evidence to show a causal relationship between exposure and cancer.
>
> Group B - Probable Human Carcinogen - limited evidence of carcinogenicity in humans and sufficient evidence in animals.
>
> Group C - Possible Human Carcinogen - Limited evidence in animals or in short-term tests.
>
> Group D - Not Classified - Inadequate animal data.
>
> Group E - No Evidence of Carcinogenicity for Humans - Negative results in at least two acceptable animal or epidemiological studies.

B. Predictive Models

Estimation of the potential human health effects of chemicals released from hazardous waste disposal activities requires three kinds of information: (a) data on the expected conditions of environmental exposure; (b) data on the response under known exposure conditions from the health effects literature; and (c) methods for predicting effects at expected exposures by extrapolation or other extensions of the literature base. This section notes the several types of extrapolations that could be required, then reviews and compares several mathematical models and other approaches for making predictions.

1. Types of extrapolations needed: Extrapolations, interpolations, or other syntheses from a data base can be required to predict qualitatively the nature of the adverse effects in humans, but will more often be needed to predict the quantitative response. If all of the human health effects to be assessed have not been identified, their prediction will be the first activity. It is vitally important, for example, to know whether a given exposure posed an immediate threat of death or severe illness, a short-term threat from accumulative concentrations, or a long-term threat of cancer. The

human health effects usually can be identified with reasonable confidence if toxicological test data in animals or other organisms are available for the test chemical or for cognate chemicals (i.e., other chemicals with similar chemical structure and physicochemical properties), or if toxicokinetic (pharmacokinetic) information is available on the chemicals' absorbability, mobility, and biotransformations within the human body or other appropriate species.

The primary need is to predict the degree of the effect of concern at expected exposure conditions based on the different set(s) of exposure conditions reported in the studies found in the literature. These predictions almost inevitably will require the extrapolation of a dose-response function across two or more sets of conditions. These include extrapolations across exposure routes, frequencies, continuities, durations, and dosages; extrapolations from test species to humans; and extrapolations from toxicological test data on individual chemicals to the exposures to complex mixtures of chemicals frequently found in hazardous wastes. A considerable literature discusses and compares methods for making such extrapolations under various circumstances and the uncertainties inherent in them. Although critical review of this literature is beyond the scope of the present discussion, the overview below may be helpful to the reader.

a. Predictions across exposure routes: The toxicity of a given chemical may vary substantially depending on how an animal is exposed to it. Factors influencing this variation include differing absorbabilities across different body membranes at point of contact, different pathways within the body that affect distribution, metabolism, storage and excretion, and ultimately different concentrations of the toxic molecules at the cells of the most susceptible (or target) organ. For many chemicals, the toxic response for the most common dosage routes generally decreases in the following order: intravenous, intraperitoneal, intramuscular, implant, subcutaneous, inhalation, oral (by gavage, water, or feed), ocular, and dermal.

In extrapolating dose-response data across exposure routes, an assumption can be made as a first approximation that the routes are equivalent. Improved extrapolations should be possible by using some of the scaling factors or convenient rules of thumb that toxicologists have developed for comparing doses by different routes. Further improvements should be possible by considering information on the nature of the toxic effect and the properties of the chemical.

b. Predictions across dose variations: The toxic response to a given chemical will vary with the frequency, continuity, and level of exposure. Although metabolism can differ at different dose levels, as discussed by Gehring et al. (1979) and O'Flaherty (1985), a conventional controlled toxicology or epidemiology study usually yields a dose-response relationship like one of those shown previously in Figure VIII-1. Extrapolations and interpolations are relatively simple if extensive controlled dose-response data are available and the environmental exposure is in the same general range. The conversion may be made graphically or by fitting a curve to the data mathematically, and then calculating the expected response at the dose of interest. Two special problems may occur: (a) the temporal aspects of the expected exposure may be different from those used in the controlled studies; and (b) the exposure levels expected may be well below doses used in the controlled study.

(1) Temporal extrapolations: If the frequency, continuity, or duration of the expected exposure differs from the frequency, continuity, or duration used in the controlled studies, the health effects may be quite different, even if the total doses seem to be roughly equivalent. For relatively small differences the time-weighted average of the exposure may be used as a first approximation to estimate the expected response from the test data. Time-weighted averages have been used with good results in many applications. An improved estimate may be possible by considering information on the specific chemical and the effect of concern. For example, the chemical may be metabolized rapidly or may tend to accumulate in certain organs; the effect may be readily repaired by the body, or injury may be cumulative. In such cases, one may defensibly adjust the simple prorating method to give an "effective dose."

Extrapolation of the results from short-term studies to long-term exposures is a difficult step because, among other problems, some effects (e.g., carcinogenesis) are seen only in longer term studies (see Schneiderman, 1981, Griffin et al., 1981 and Hertzberg and Dourson, 1983; and Hertzberg, 1984). Conversely, certain responses sometimes can be determined better with acute or subchronic rather than chronic exposures. For example, teratogenicity is usually best determined with a few repeated doses during early pregnancy. Some research results suggest that the chronic toxicity of a chemical can be partially estimated from subchronic and acute toxicity tests on it, and from general toxicological principles. These results are worth noting. This subject is discussed further later in this section.

(2) High dose to low dose extrapolations: As noted in Section A, quantitative extrapolation at low doses can be difficult, both for relationships that exhibit threshold and those that do not. A particularly difficult problem occurs if the expected exposure is below an observed "minimum effect level" in the controlled studies of a carcinogen. Arguments have been made on biological and statistical grounds that threshold levels do not exist for exposures to chemical carcinogens,* that any exposure, no matter how small, poses some small risk of cancer. Similar arguments could be (but generally have not been) made in regard to the occurrence of mutagenic, teratogenic and many other effects at very low doses. Biological rationales have been suggested in support of a threshold level for some effects (Cornfield, 1977). As noted previously, however, a conclusion on a threshold's existence for most morbidity and mortality effects is largely a matter of faith (or probabilistic degree of belief) in the rationale.

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* This theory was first based on a similar theory developed in the 1950s regarding the carcinogenicity of ionizing radiations, particularly radioactive nuclides. Excess exposure to X-rays was considered to cause cancer as early as 1902 (GAO, 1981).

For carcinogens, mathematical models have been extensively studied as aids in predicting cancer risks at very low doses, as will be described in Subsection B.2. These models may be useful for other non-threshold effects. For effects for which a threshold is assumed, risks down to threshold can be estimated by graphical or mathematical models incorporating a specified threshold. In addition, several other predictive approaches have been reported, including: toxicokinetic models, quantitative structure-activity relationships (QSAR), prototype relative potency methods, nonparametric methods, and extrapolations from in vitro test data with microorganisms and cell cultures. These other predictive methods are also discussed later in this section.

c. Predictions across species: No rigorous scientific basis exists for general quantitative extrapolation of animal test data results to humans, and many problems exist in making predictions. Such extrapolations require making two kinds of assumptions: (a) that a method is available for determining equivalent doses in two species, and (b) that a method is available for determining the response in the two species at equivalent doses.

(1) Dosage conversions: The dose units used should enhance interspecies comparison, and be readily calculated from available data, if not used explicitly in the original study. Two types of does units are commonly used in the literature:

- Concentration-in-medium (e.g., parts per million in feed, mg/m^3 air).
- Quantity per animal on either a weight basis (e.g., mg/kg, mmoles/kg), or surface area basis (e.g., mg/m^2, mmoles/m^2).

All are used in various studies, and each can be converted relatively easily to the others, with proper conversion factors. Therefore, the units of choice should be based on their biological usefulness. The basic biological phenomenon involved is the reaction of the toxicant molecule with a biological molecule (usually called a receptor) located at an active site, initiating a series of reactions, ultimately resulting in an observable effect. As described in more detail by Gilman et al. (1980), this sequence seems to follow chemical mass-action laws, so choice should be based on the characteristics of the receptor reactions.

The concentration-in-medium measure has been found most useful in toxicology for situations involving a direct contact between the medium and the receptor tissue, e.g., irritation of skin by liquids or of respiratory organs by gases. In risk assessment, the exposure analysis frequently yields results as concentration-in-medium. These can sometimes be used directly, e.g., Alarie (1981), assessed the acute irritation of nose and lungs by airborne chemicals.

With most biological systems, the situation is more complicated, since the chemical must enter the body (via the respiratory tract, the skin, or the gastrointestinal tract), be transported to its active site (usually through the blood), and then react with the receptor. While the chemical acts on the body, the body also acts on the chemical, converting it to other chemicals (metabolism) and excreting it by various pathways (air, bile to feces, urine, sweat). (For an overview, see the introductory chapters of Doull et al. (1980) and Gilman et al. (1980).)

When comparing chemicals, one may refine the dosage estimates by the use of moles in lieu of simple weight, although biological variation is often so great that this does not improve precision. Therefore, the basic question remaining is whether to use mg/kg body weight or mg/m^2 surface area.

The traditional units are mg/kg. They are simple, straightforward, and widely accepted. Recently, however, a surface area relationship was suggested (Mantel and Schneiderman, 1975) and was adopted by EPA in its water quality criteria documents (EPA, 1980c). For simplicity, the surface area usually is assumed to be proportional to the two-thirds power of body weight. (The assumption holds for most mammals, but somewhat underestimates the surface area of long-limbed monkeys.) This scaling system compresses the interspecies dose range (see Klaassen and Doull, 1980), and is preferred by some authorities (such as Albert, 1980), but not by all (such as Morris et al., 1982). It has the advantage that many metabolism functions (such as calorie and oxygen intake) are best correlated to weight by a power close to two-thirds. The only studies comparing the weight and surface area units involve anticancer drugs, which find the surface area units superior (NRC, 1980a).

Table VIII-2 gives a set of average characteristics for humans and several species that are useful in calculating equivalent toxicity test doses and other interspecies comparisons.

(2) Nature and extent of response: At nominally equivalent exposures, different species may respond differently in both nature and degree. The occurrence of some types of effects in humans is difficult to predict confidently from valid results reported in the literature. For example, common table salt caused substantial teratogenic effects when injected in a large dose (2,500 mg/kg) under the skin of mice in the 11th day of gestation (Nishimura and Miyamoto, 1969). The effect of corresponding doses on humans is unknown, but no evidence exists for effects at normal salt consumption rates. In contrast, thalidomide is not teratogenic in rats, but is in rabbits, monkeys, and humans at moderate doses (Wilson, 1971). The effect identification problem is not discussed further here, but some of the methods used for identification are also used to estimate dose- response relationships and are addressed subsequently.

Humans are known from clinical observations, controlled experimentation, and epidemiological studies to have many but not all of the responses of typical laboratory animals to exposures to a great many chemical substances. The clinical observations usually give information on response at

TABLE VIII-2

USEFUL FACTORS FOR INTERSPECIES COMPARISON

Species	Weight (kg)	m^2/kg	Surface Area (m^2)	kg/m^2	Food/Weight Fraction[a]	Water/Weight Fraction[b]	Respiration Rate[c]	Lifetime (days)
Mouse	0.030	0.340	0.0102	2.94	0.13	0.17	0.04	550
Hamster	0.125	0.212	0.0265	4.72	0.12	0.68		910
Rat	0.35	0.150	0.0525	6.67	0.05	0.078	0.24	910
Guinea pig	0.40	0.114	0.0575	7.0	0.028	0.34	0.07	730
Rabbit	2.00	0.084	0.168	11.9	0.049	0.081	1.6	2,000
Cat	3.00	0.073	0.220	13.6	0.030	0.097	1.5	5,100
Monkey	4.00	0.067	0.267	15.0	0.042	0.13	1.3	5,500
Dog	12.0	0.046	0.555	21.6	0.029	0.025	1.5	5,500
Human	70.0	0.026	1.800	39	0.028	0.030	20	25,600

Sources: Durkin (1982); EPA (1980a) (1983); and MRI calculations. The latter assumes

$$m^2 = 0.106\ (\text{wt in kg})^{2/3}.$$

[a] Wet weight of feed consumed each day divided by body weight.
[b] Drinking water consumed each day divided by body weight.
[c] Cubic meters of air per day.

high exposures, but little if any quantitative information on dose-response function at moderate and low doses.

The experiments necessary to obtain human data are usually precluded by ethical considerations and legal restrictions. Results of some epidemiological studies are available (including occupational, environmental, and consumer exposures) on the effects of some chemicals on humans, but these are often difficult to interpret because of confounding factors (e.g., mixtures) and data gaps. Such studies usually begin after the adverse effects has been noted and long after the toxicant has dispersed; therefore, few, if any, dosage data are available. Occupational health effect studies may even include good data on toxicant levels in the vicinity of work stations, but actual exposures may be uncertain because of wide variance in work practices and human behavior. However, in those cases where human data are available, they should be used to determine dose- response functions, or at least to verify that humans also incur the effects of concern observed in animals.

Crouch and Wilson (1979); Crump et al. (1985); Clayson (1985); Hart and Fishbein (1985); and Withey (1985) have recently discussed the possibilities and difficulties of interspecies extrapolations. The unique susceptibility of the mouse liver to carcinogenic response to chemicals that do not have activity in other mouse organs or in rats or other test species has been well documented (Periera, 1985). In general, extrapolation to humans can be made most confidently from other primates, then (in approximate order) from the larger test mammals, rodents, fowl, plants, and microorganisms. On the other hand, an extensive data base has been developed in the last two decades on the mutagenicity in bacteria of many chemicals believed to be mutagenic and carcinogenic in humans (Ames et al., 1962; Ames et al., 1973. These and other in vitro short-term tests were recently reviewed (Hollstein et al., 1979); they are also noted subsequently in the subsection "Other Predictive Methods."

In the absence of information to the contrary, an assumption is usually made as a first approximation that the response in humans and in test animals is the same at equivalent doses. This assumption could lead to substantial overestimates of human risk in many cases, but might lead to underestimates in others.

d. Extrapolations to mixtures of chemicals: Hazardous wastes pose a special problem in health effects assessment because they usually contain more than one toxic chemical. Thus, the usual situation involves exposure to several chemicals more or less simultaneously. Almost all the available health effects data, however, are from experimental studies of exposure to a single, relatively pure chemical. Thus, one must consider how to estimate the effects of mixtures by using data for single chemical exposures.

A few recent studies consider the problem of mixtures in some detail. The National Research Council (NAS/NRC, 1980a) attempted to assess the hazards of exposure to multiple chemicals in a marine environment. In a later report (NRC/NAS, 1982), the Council published a symposium on the state of the art in assessment of multichemical contamination, which provides a good summary of the limited knowledge of methods for study of simultaneous exposures.

The EPA's Environmental Criteria and Assessment Office (ECAO) in Cincinnati has been developing a multichemical health risk assessment methodology which can be used in conducting site-specific risk assessments on hazardous waste disposal facilities. Proceedings of an ECAO workshop held in Cincinnati, Ohio, in 1982, are available (EPA, 1984a), as are draft proceedings from a second workshop held there in 1983 (EPA, 1983). In 1986 EPA published guidelines for risk assessment of chemical mixtures (EPA, 1986d).

Calle et al. (undated) of the Oak Ridge National Laboratory considered health effects assessments of the complex mixtures in synfuels, and recommend that such mixtures be treated as if they were single chemicals (i.e., be tested and evaluated as such). The U.S. Department of Energy's Health and Environmental Risk Analysis Program conducted a workshop on risks from mixtures of chemicals. A summary of the workshop (DOE, 1983) concluded that the relative potency of a substance in various animal systems was useful in estimating human risk. It recommended the use of multiple short-term tests of many chemicals and mixtures to estimate their relative potencies as carcinogens, in lieu of conducting the more lengthy and costly long-term tests necessary to determine potencies of each directly.

Christensen and Chen (1985) have derived and tested preliminarily noninteractive multiple toxicity models for quantal response of organisms to two toxicants, using probit, logit and Weibull transformations for the tolerance distributions of each. Only the nonnormally distributed Weibull model gave an acceptable fit to experimental data.

For even the simplest mixture (only two chemicals), there are three possible cases: additivity, synergism, and antagonism. In additivity, the effects of the two chemicals are separate and noninteracting, so the observed effects are the sum of the individual effects (response addition) or the effect of the net dose (dose addition), where the latter is a weighted sum based on each substance's relative potency. In synergism, the chemicals interact so that the total effect is greater than the sum of the individual effects. Several types of synergistic interactions have been well-documented. A simple case is the increased penetration of body membranes (skin, stomach lining, placenta) by some toxic chemicals when certain other chemicals are present. A number of chemicals that are not themselves necessarily carcinogens may act as promoters* and increase the carcinogenicity of other substances. One of the most notorious promoters is tobacco smoke, which is highly synergistic with other lung irritants, such as asbestos fibers, as well as being carcinogenic by itself. In antagonism, the combined effect is less than the sum of the individual effects. This phenomenon is often sought in the development of antidotes and other therapy against toxic effects. With both nonadditive cases, the parameter of interest is the degree of interaction; this may be a constant or may be a function of dose.

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* Cancer promoters are sometimes referred to as epigenetic agents. Substances which cause irreversible changes themselves, thereby initiating a carcinogenic process (initiators), are often referred to as genotoxic agents. Some authorities have protested that the use of this terminology should be limited to distinguishing modes of action, and should not be used to classify chemicals, since a given chemical may act at times by either mechanism.

If interactions exist, the health effects of sequential and simultaneous exposures are likely to differ. In addition, different permutations of sequential exposure may have different effects. Further, the response variance may be greater between individuals for exposure to mixtures than for exposure to a single chemical.

In the absence of specific studies, one cannot predict which case will apply to a given mixture. The common practice, therefore, is to assume the effects (or doses) of different chemicals to be additive. This is the simplest case, since estimates of the degree of interaction are not required, and is also the median case among the three (i.e., neither best nor worst case). Thus, unless specific information is available, the effect (or dose) of each chemical is usually considered separately, and the estimated adverse effects are aggregated at the end. It is possible that one or a few components will be sufficiently potent and in such high concentrations that it or they dominate the observed adverse effects. If so, the risk estimation can ignore the less potent chemicals without affecting its validity significantly (i.e., without affecting the uncertainty level).

In the rare cases where it is known that there are interactions, and these interactions have been quantified, this knowledge can be incorporated into the risk estimation. If the data allow, the doses of the various interacting chemicals should be combined into a single "effective dose" and used as the dose variable in the usual methodology.

2. Mathematical extrapolation models: Toxicological extrapolation models can be divided into three major classes and several subclasses. Mathematical models for extrapolating (or interpolating) response (or risk) across dosage, and particularly from high to low dose have received the most attention from regulators; consensus does not exist on their reliability at very low dose. Toxicokinetic (or pharmacokinetic) models are potentially more versatile (e.g., applicable across dose, route, species, etc.); they are limited in use by their specificity and data requirements. The third class is a collection of approaches that may be useful when data needed in other approaches are inadequate; they might be used for quantitative assessment, but would probably be limited by the data base to a qualitative output.

a. Difficulties in modeling: Modeling of many biological effects is difficult, but attempts to model carcinogenesis mathematically have proved to be exceptionally so. Efforts to apply mathematical expressions to toxicological dose-response relationships began in the 1930's with the work of Gaddum and Bliss on acute quantal response data (Brown, 1985). The now familiar probit model (see below) became a standard tool in estimating LD_{50}s. The discovery that ionizing radiation could cause cancer led in the 1940s and 1950s to extensive research on dose-response functions for low dose predictions (NRC/NAS, 1972). The results of this work has had great influence on attitudes towards assessing and managing the risks not only of radiation, but also of chemical carcinogens (NRC/NAS, 1980b; Woodhead et al., 1985). Many models for extrapolation to low dose for carcinogens (and other toxicants) have some basis in early theory of radiation effects. Recent discussions have noted the substantial differences (as well as the similarities) in carcinogenesis by radiation and chemicals, both in molecular mechanisms (Borg, 1985) and in cellular or animal models (Fry, 1985).

The mechanisms of carcinogenesis have been difficult to elucidate and this difficulty accounts for the suggestion and evaluation of many increasingly complex models over the past 30 years (Whittemore and Keller, 1978; OTA, 1981; OSTP, 1985; Brown, 1985; Borg, 1985; and Fry, 1985). Current consensus is that at least three major phases occur in the development of cancer: initiation; promotion or expression; and progression. A given chemical may be an initiator, a promoter, or a complete carcinogen.

An initiator appears to cause a rapid, irreversible heritable change in a target DNA molecule or cell in a target organ. The reaction appears to be first order kinetically without threshold. The change can lie latent (even long after the chemical has been eliminated) until promotion occurs, unless the cell dies or is destroyed by bodily safety mechanisms. Promotion is less well understood, and may have multiple forms or stages involving possibly both direct and indirect mechanisms. A promoter (of which there are many*) appears to alter the differentiation capability of an initiated cell, possibly through adduct formation, amplification of damaged or normal genes, or activation of repressed genes. A promoter's effects are susceptible to bodily repair mechanisms, and the promoter must be present on an extended basis (repeated or chronic exposure) to result in tumors. (Tumors may regress if exposure ends). Cells that have been initiated/promoted may still die or be constrained by the tissue's cell system. In the progression stage the cell apparently undergoes sufficient genomic change (e.g., perhaps through chromosomal translocations) that it largely escapes control by the surrounding tissue and proliferates unrestrained. Promoters may at times be required to maintain progression, since tumors will occasionally regress when exposure to a given carcinogen is stopped.

In addition to uncertainties about the mechanisms of a given carcinogen, the subject organism is also invariably being subjected to many other cancer-related agents, including initiators or promoters (possible cocarcinogens) and also anticarcinogens. Ames (1983) has described a plethora of natural mutagens and carcinogens in the normal diet. Many of these chemicals act through generation of oxygen radicals which may play a degenerative roll in cancer, heart disease, and aging. The intake of these agents is compounded by the lifetime exposure to naturally occurring radioisotopes and intense cosmic rays. The diet also contains chemicals believed to act as anticarcinogens.

Considerations of the uncertainty in the effective dose of the carcinogen, coupled with uncertainty in the carcinogenesis and bodily repair, as partially summarized in Figure VIII-3, reveal why epidemiological and

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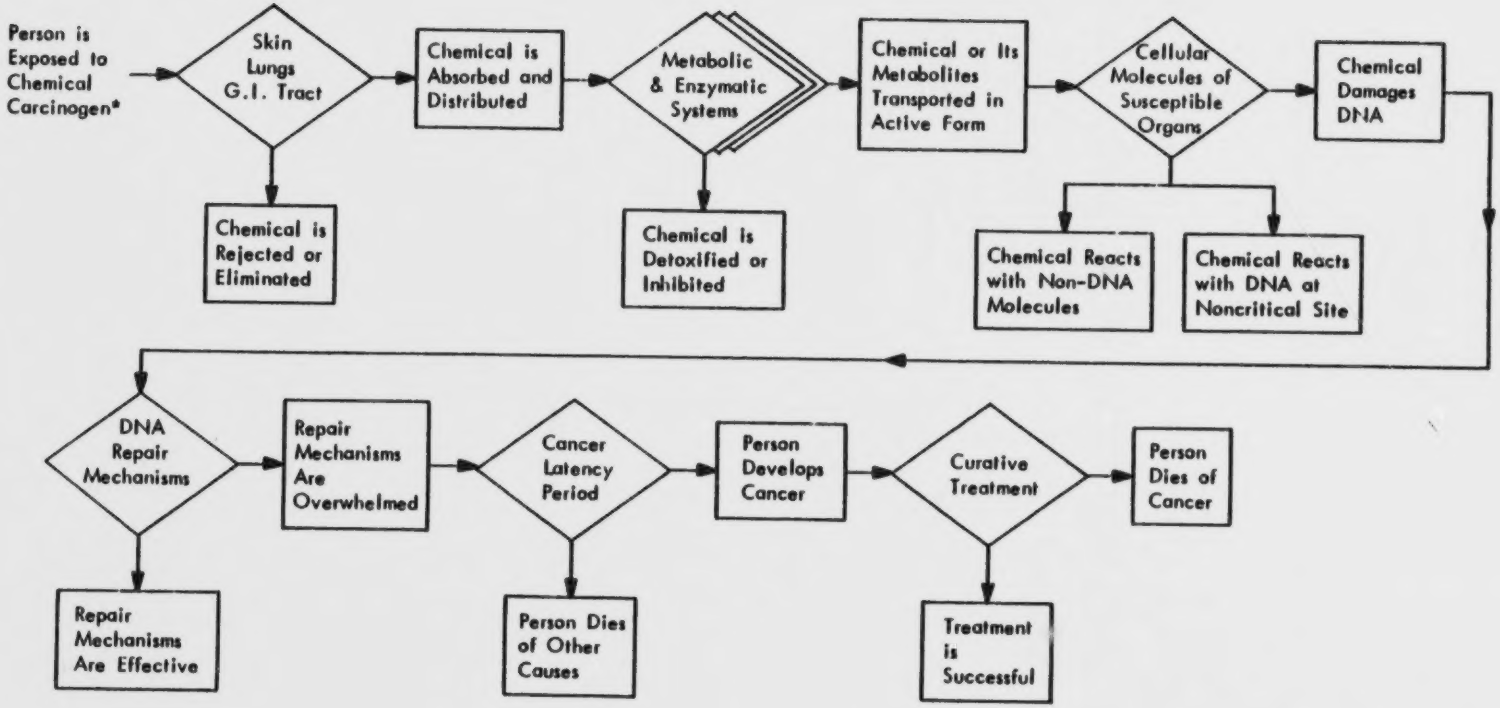
* The common amino acids (such as trytophan, leucine, and isoleucine), present in proteins, saccharin, and the sodium salt or ascorbic acid (Vitamin C) have all been found to act as promoters.


Person is Exposed to Chemical Carcinogen*
Skin Lungs G.I. Tract
Chemical is Rejected or Eliminated
Chemical is Absorbed and Distributed
Metabolic & Enzymatic Systems
Chemical is Detoxified or Inhibited
Chemical or Its Metabolites Transported in Active Form
Cellular Molecules of Susceptible Organs
Chemical Reacts with Non-DNA Molecules
Chemical Reacts with DNA at Noncritical Site
Chemical Damages DNA
DNA Repair Mechanisms
Repair Mechanisms Are Effective
Repair Mechanisms Are Overwhelmed
Cancer Latency Period
Person Dies of Other Causes
Person Develops Cancer
Curative Treatment
Treatment is Successful
Person Dies of Cancer

*May include cocarcinogens, synergists, activators, etc.; exposure may be repetitive.

Source: Lawless, Edward W., Midwest Research Institute
(unpublished, 1978)

Figure VIII-3 - Factors that Modify the Death Rate from Exposure to Chemical Carcinogens

toxicological studies often yield dose-response data that are difficult to interpret with general mathematical models.

b. Dose-response extrapolation models: Mathematical extrapolation from high dose levels to low dose levels is usually required to estimate human health risk. Typical laboratory toxicity studies involve 10 to 100 animals per dose level because of logistical limitations. The sensitivity of the test is arithmetically limited to an effect of 1 to 10% incidence in test animals dosed at levels high enough to produce an observable effect, and cancer risks below 1% cannot be measured in animals with any useful degree of accuracy (Crump, 1981b; Cairns, 1979).* However, most risk assessments require the evaluation of effects with lower incidence, such as 1 to 10 in a million (i.e., 10^{-5} or 10^{-6}). Therefore, an extrapolation to the expected very low level exposure is required. For this reason both the response (risk) and dose are usually placed on logarithmic scale.

A variety of models is available to make extrapolations, although in modeling research heavy emphasis has been placed on two areas: acute lethal doses and carcinogenesis. Most of these models were developed over 20 years ago. The models and their biological rationales are discussed in several references (Food Safety Council, 1980; NRC/NAS, 1980b; Altshuler, 1981) Munro and Krewski, 1981a, 1981b; Krewski and Van Ryzin, 1981; Richmond et al., 1981; Tardiff and Jaffe, 1982; Park and Snee, 1984; Bickis and Krewski, 1985; Crump, 1981, 1985a, 1985b; and Brown, 1985). Krewski and Brown (1981) also provide a bibliography of the carcinogenic risk assessment literature.

Although not always expressly stated, most of the models have variants to allow elimination of background rates (i.e., the presence of adverse effects in undosed control animals). Thus, what is usually calculated is the additional risk resulting from exposure over the normal or background effect level. In addition, threshold doses, if known, could be incorporated in most of the models, although this is not done frequently.

In general, all mathematical models assume that the probability of response (P) at a given dose (d) is a function of the dose

$$P(d) = f(d)$$

but differ in the functional relationship. Four subclasses of such models are discussed below and then briefly evaluated.

(1) Simple algebraic models: In the simplest case, the function is linear over the entire range of doses

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* The ED_{01} study, the largest animal study to date, was designed to estimate with precision the dosage of a very potent carcinogen that would produce an increase in tumor incidence of 1%. It used over 24,000 mice (Cairns, 1979).

$$P(d) = a \cdot d$$

where the constant, a, is the slope of the dose-response line.

The linear relationship can be modified to include either or both a background incidence $P(d_o)$ and threshold dose (d_t).

Linear models $P(d) = P(d_o) + ad$

$P(d) = a(d-d_t)$

$P(d) = P(d_o) + a(d-d_t)$

where the effective or excess* probability, Pe(d) is:

$$P_e(d) = P(d) - P(d_o).$$

This method of correcting the response for background is satisfactory for many purposes, particularly if the background incidence is small. Better comparisons can be made between response probabilities or risks found in different studies, where differing (and sometimes high) background levels exist, by converting the responses above background in each data set to new 0 to 1.0 scales. A formula, known as Abbott's correction, expresses the risk as:

$$R(d) = \frac{P(d) - P(d_o)}{1 - P(d_o)}$$

A straight line can be fit to a data set by regression analysis and used for predictive purposes, including extrapolation to estimate the threshold dose or background incidence. Few data sets are linear over the entire range, however, and more complex functions required consideration. For example, the four models below have been tested on the effects of ionizing radiation (NRC/NAS, 1980b; GAO, 1981):

Square Root Model $P(d) = P(d_o) + ad^{\frac{1}{2}}$

Quadratic Model $P(d) = P(d_o) + a_2d^2$

Cubic Model $P(d) = P(d_o) + a_3d^3$

Linear Quadratic Model $P(d) = P(d_o) + ad + a_2d^2$

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* In the literature, $P(d) - P(d_o)$ is variously called the added, additional, increased and excess probability (or risk).

The linear no-threshold model gave a reasonably good fit to some data sets involving cancer incidence following radiation, particularly for so-called high-LET radiation* such as alpha particles (helium nuclei), protons and fast neutrons and cosmic rays (heavy nuclei), but a poorer fit for low-LET radiation beta rays (electrons), gamma rays, and X-rays.** These data in many cases were based on epidemiological studies following high dose, multiple type, whole body, radiation (e.g., atomic bomb survivors at Hiroshima and Nagasaki). Land (1985) recently reviewed the difficulties in extrapolating cancer risks from such large-scale radiation exposure.

The National Research Council's Committee on the Biological Effects of Ionizing Radiations have considered these effects at length (the so-called BEIR Committee reports: NRC/NAS, 1972, 1977b, 1979, 1980). The 1972 BEIR report used the linear model to estimate cancer induction at low doses of radiation, and this model became the basis of current radiation protection standards. In 1980, however, the BEIR Committee members could not reach consensus: most members now believed that although the linear model was satisfactory for high-LET radiation, the linear-quadratic model was best for predicting low LET low dose risks. One dissenting opinion (that of the committee chairman) favored the linear model for all radiation, while another opinion favored a pure quadratic model because the linear model overestimated risks at low dose LET, but might underestimate neutron hazards.

These deliberations are important to the present study of risks from chemical carcinogens. Although chemical carcinogens are very low energy sources compared to ionizing radiation or even to ultraviolet light, the concept that the dose-response relationship for chemical carcinogens should be linear, at least at low doses, became widely accepted for regulatory purposes. In fact, a "linear interpolation model" developed by Hoel et al., 1975 (see below), and briefly adopted by the EPA in 1976 for carcinogen risk assessment, drew heavily on the linear model endorsement in the 1972 BEIR report. While most models for extrapolations of chemical risks are more strongly based on toxicological theory and experience than these simple algebraic models, all the models currently favored for low dose carcinogenesis prediction incorporate near linearity at low dose with no threshold. On the other hand, the kinetics of metabolic processes other than those directly involved in carcinogenesis can probably cause deviation from linearity at low dose. In fact, Doll and Peto (1978) observed that a quadratic dose-response relationship provided a better fit for data on lung cancer and smoking than did a linear model.

(2) Tolerance distribution models: This class of models is based on the deterministic view that for a toxic substance each individual

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* LET (linear energy transfer) refers to the amount of energy an ionizing particle gives up per unit length of track in receiving material.

** Ultraviolet rays are essentially nonionizing in biological media, but can cleave molecules into reactive free radicals that initiate cancer. Ultraviolet rays are particularly associated with skin cancers. Cosmic rays contain a broad mixture of electrons, mesons, protons, and heavier particles.

has a tolerance level which, if exceeded, always causes the effect, and on the assumption that a distribution of tolerances exists in the test population. Different distributions lead to the probit and logistic models.* Tolerance distribution models suggest assumption of a threshold dose for each test subject, but do not preclude vanishingly small thresholds for specific subjects.

Probit model--The basic probit** model assumes a normal distribution of events. For toxicological dose-response applications, a log-normal distribution of individual tolerances is assumed. The model is sometimes called the probit log-dose, log-probit and log-normal models, as well as the probit model. The equation for probability of response versus dose is:

$$P(d) = (2\pi)^{-1/2} \int_{-\infty}^{\alpha + \beta \cdot \log d} e^{\frac{-u^2}{2}} \, du$$

where $P(d)$ = probability of effect at dose d

$u = \log x$, where x is the variate of the classical bell-shaped normal distribution, and
α = parameter to be estimated, and
β = parameter to be estimated (called the slope of the probit line), where $\beta > 0$.

Originally developed in drug development research to fit research data for acute exposures, the probit model is very useful in obtaining the LD_{50} by interpolation, since it can be applied with only one dose level plus a control group. The model is not highly flexible in fitting data, but the log-probit model adequately fit the observed data for both liver and bladder cancers in the ED_{01} study (Farmer et al., 1980).

The probit model curve is convex in the 10 to 50% response range, but the response approaches zero rapidly at low dose. It is inherently nonthreshold, but is concave in extrapolation to very low dose on a log-log scale. It almost always yields lower estimates of risk at low dose than do other models.

Mantel and Bryan (1961) adapted the probit model to estimate "safe doses" of carcinogens. In this method, the parameter β was not estimated from the data, but was set arbitrarily to unity (presumed to be a conservative procedure). Other parameters are then varied to give an upper 99% confidence level on the risk at a given dose. The safe dose is then defined as the dose expected at the 99% confidence level to give no more than an assigned very low response, such as 10^{-8} The U.S. Food and Drug Administration adopted the log-probit model for a time around 1970 in support of its regulation of carcinogens. This procedure was subsequently improved (Mantel et al., 1975), and was specified by EPA in 1976 as one of two models (the other being the one-hit model) in its interim guidelines for assessing health risks of suspected carcinogens. It has been criticized, however, on the theoretical grounds that it ruled out linearity at low dose (a feature viewed as essential by Peto, 1974), gave a poor fit to data because of its concave curvature, and eventually underestimated risks when extrapolated to very low doses (Crump and Masterman, 1979). In particular, it was not sufficiently "conservative." In addition, the version of the probit model that incorporated a background level of cancer implied that the mechanisms of background and dose-induced tumors were independent (Crump et al., 1976; Crump, 1977 and 1979; Hartley and Sielken, 1977; and Salsburg, 1979). This model is no longer highly regarded for regulation of carcinogens by the FDA or EPA, but the Mantel-Bryan concept of extrapolating upper confidence limits has been used with other dose-response models.

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* The Weibull model is sometimes grouped with these models, but is better classified with mechanistic models as will be seen in Section B.2.a.3.

** Probit is an acronym for the term probability unit. The probit scale is based on deviations from the mean of normal distribution; the scale is adjusted to avoid negative numbers.

In addition, Hattis (1987) notes that probit risk assessment formulas used for chlorine gas releases by different groups differed by over a factor of 10 in the LD_{50} for humans, which then (because of the highly nonlinear nature of this function) led to a billion-fold difference in population mortality risk in the region of the more conservative LD_{50}.

Logistic model--The "logit" model (developed about 1944) uses the log logistic distribution rather than the log normal distribution of the log-probit model; otherwise the models are similar, and the logit yields a sigmoid-shaped curve also. The equation is:

$$P(d) = \frac{1}{1 + e^{-(\alpha + \beta \cdot \log d)}}$$

where $\beta > 0$

In low dose extrapolations, this model can be linear ($\beta = 1$), sublinear ($\beta > 1$) or supralinear ($\beta < 1$). The logit model usually gives risk estimates at low dose somewhat higher than those of the probit model. The logit model is used in mathematical models of many growth processes, but has not been applied as much as some of the other models in health risk assessment of chemicals. In contrast, the multiple logistic model of Truett et al. (1967) has become the dominant model for analysis of cardiovascular disease. The equation is:

$$R = \frac{1}{1 + e^{-(\beta_0 + \beta_1 X_1 + \ldots \beta_k X_k)}}$$

where R is the risk of developing a particular cardiovascular disease over time, the βs are constants, and the Xs are the raw levels of such risk factors as age, blood pressure, cholesterol level, etc.

(3) Stochastic mechanistic models: Models in this class all assume a degree of randomness in events leading to response, but also have some basis in toxicological theory. These models all assume that a certain number of reactions, events, or "hits" (a term used in radiation carcinogenesis theory) are necessary between molecules (or fragments of molecules) of a toxic substance and a cell or molecule within a cell of the victim to produce the effect. One should note that in the original development of all these models, response was considered as a function of time, but most are now more familiar in their dichotomous dose-response forms.

One-hit and linear extrapolation models--The one-hit model of carcinogenesis was proposed by Iverson and Arley in 1952 (NRC, 1977a). It assumes that a single biologically effective dose reacting with one receptor site within a cell is adequate to cause a transition to a cancer cell, which then multiplies at a rate independent of the initiating dose until a tumor is detectable. A "hit" can be considered to be one or more of a variety of possible fundamental biological events, within a specified interval of time, including, in the extreme the reaction of a single toxicant molecule with the DNA of a single cell in the organism. If the number of hits in the interval follows a generalized homogeneous Poisson process, then the equation for the probability of response for an individual is:

$$P(d) = 1 - e^{-\beta d} ,$$

where βd = expected number of hits at dose d, ($\beta > 0$)

This is the one-hit model, sometimes called the simple exponential model. At very low doses, the relationship becomes:

$$P(d) \simeq \beta d$$

Background response levels can be taken into account in this and most other models by assuming that they are either independent or additive to the response to the test substance (Hoel, 1980). The calculations differ,* but in general:

$$P(d) = 1 - e^{-(\alpha + \beta d)}$$

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* If the response to stimulus is assumed to be independent of the background, Abbott's correction is used. If the stimulus is assumed to have a mechanism similar to that causing the background, then it is added to an assumed effective background dose. Extra risk calculated at low dose by the two methods can differ by several orders of magnitude.

where α reflects the background. A version of the one-hit model that incorporates a threshold can also be written (NRC/NAS 1977a):

$P(d) = 1-e^{-\beta(d-d_t)}$ where d_t is the threshold dose.

Unfortunately, the one-hit model often is called the linear model. In fact, the line fitted to dose-response data with this model is slightly concave, although its extrapolation to low doses becomes nearly linear. Because the model has only one parameter, it is not flexible in fitting the typical sigmoid-shape of a rich data set. The parameter can, however, be obtained if only a single positive response dose point is available by using the origin of the dose-response graph (or background) as a second point. In practice, if the fit of the curve to the full data set is unsatisfactory (e.g., by the chi-square statistic test), high dose data points are dropped successively until a fit results, even if only one positive point remains. The slope of the curve below the lowest data point and an assumption of linearity can be used with a nonintercept log-log scale to estimate risks at very low doses or a "virtually safe dose" (VSD) where the risk was say $< 10^{-6}$ (Crump et al., 1977), i.e., a de minimis risk. Confidence limits of the line also can be extrapolated. The choice of confidence limits is arbitrary but 99%, 95%, or possibly 68% are common. Because of its desirable features, intensive efforts were made during the 1970's to justify this model and use it in regulations of carcinogens.

The U.S. Food and Drug Administration adopted a version of this model in 1971 to make conservative estimates of risk at low dose; FDA chose to use linear extrapolation of the upper 99% confidence limits. Following the BEIR committee's 1972 conclusion that radiation-induced cancer was a linear function (NRC/NAS, 1972) and Peto's insistence that the dose-response curve must be linear with positive slope as it approaches zero dose (Peto, 1974), a National Research Council Committee endorsed linear extrapolation for carcinogens (NRC/NAS, 1975). Numerous publications contended variously that the one-hit model was consistent with biological assumptions, that any acceptable model must be linear at low dose for all directly acting carcinogens, since they would add to background incidence, and that linear extrapolation should be made using upper confidence limits (Hoel et al., 1975; Crump et al., 1976, 1977). Several papers discussed preferred methods of using low dose data points for interpolation or linear extrapolation (Hoel et al., 1975; Gaylor and Kodell, 1980); Altshuler, 1981). The U.S. Interagency Regulatory Liaison Group, following its FDA members, recommended linear extrapolation from the lowest positive data point (IRLG, 1979). The EPA adopted the one-hit model or its linear extrapolation variation for a time (1976-1979) as a basis for estimating health risks of expected carcinogens (EPA, 1976), in setting water quality criteria (EPA, 1979), in regulating pesticides (NRC/NAS, 1980) and for generally estimating VSDs for carcinogens.

The appropriateness of this one-hit model as a basis of regulation was increasingly disputed, however. Questioned were its biological basis (particularly after the BEIR committee substituted a linear-quadratic for the linear model for predicting cancer from ionizing radiation, NRC/NAS, 1979, 1980b), the toxicological instability of low-dose data points that leads to statistical instability of the low dose extrapolation,* and the conflict between some predicted response levels and those determined in epidemiological studies. While some authors suggested that the model might, with some data sets, actually underestimate low dose risks, others insisted that the high risks usually estimated produced unnecessarily adverse societal impacts when translated into regulations (see for example Cohen, 1981).** Most troubling, perhaps, was the problem of justifying use of only the lowest data point, and disregarding more reproducible midrange points when the model provided an unsatisfactory fit to the data set, as frequently occurs (Van Ryzin, 1980). When the one-hit model was applied to the results of the ED_{01}, study (see Figure VIII-2), a satisfactory fit could be obtained for only the lowest three data points for the liver tumors, and the fit to the bladder tumor data was not as good as that obtained with the Weibull model (Carlborg, 1981c; OTA, 1981). Because of the substantial credibility and practical problems with the one-hit model, the EPA's Carcinogen Assessment Group replaced it with the multi-stage model in its water quality criteria development (EPA, 1980a, 1980b, 1980c) and in other risk assessments.

The one-hit model can be regarded as a special case of the multi-hit, multistage, and Weibull models (see below) that results when appropriate parameter values are used in each (e.g., unity for k in the multistage or for m in the Weibull). Therefore, those models are more flexible in fitting data than the one-hit and better suited for regulatory use.

Rai and Van Ryzin (1985) have applied the one-hit model to teratological data, although this response is often considered to exhibit a threshold effect.

Multi-hit model--This model (first proposed by Cornfield in 1954) assumes that several events or "hits" must occur to cause response and that they follow a gamma distribution function. The equation is:

$$P(d) = \frac{1}{\Gamma(k)} \int_0^d (\beta t)^k \cdot \frac{e^{-\beta u}}{u} \, du,$$

where

$\Gamma(k)$ = the gamma function, $\int_0^\infty t^{k-1} e^{-u} \, du$

u = variable of gamma function,

k = number of hits (but not necessarily an integer).

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* The upper 99% or 95% confidence limit is more stable for a given data set for such models, even if the model's basis is disputed.

** Because of the poor fit that the one-hit model provides to good data sets, it is not surprising that it can underestimate as well as overestimate risks.

This model, frequently called the Gamma Multi-hit model, can also be considered a tolerance distribution model, but was derived from considerations very similar to those of the multistage model. It can be derived as a special case of the multistage model (Crump, 1985a) and contains the one-hit model as a special case. Rai and Van Ryzin have developed its use (Van Ryzin, 1980). The multi-hit model is much more flexible in fitting data sets than the one-hit model, but requires much more data to define the parameters. In fitting data, the multi-hit resembles a blend of the probit model at high dose and the logit model at low dose. A computer program, Multi 80, was developed by Rai and Van Ryzin (1980) for model fitting. Rai and Van Ryzin (1981) discussed applicability of a generalized multi-hit model for low dose extrapolations.

In 1978 the Food Safety Council (1978) and Rai and Van Ryzin (1981) suggested use of the multi-hit model for low dose extrapolation of cancer risks. Crump and Masterman (1979) contended that multi-hit models that are linear at low dose are necessarily curved downward at high doses, that confidence limits based on it can be either supralinear ($k < 1$) or sublinear ($k > 1$), and that lower confidence limits on VSDs from the model with $k = 1$ can differ substantially from VSDs calculated by other satisfactorily fitted curves on several data sets. Because the original version of the model assumes complete independence of background incidence, it yields with some data sets confounded estimates of background, and even of response at moderately low dose.* Haseman et al (1981) have reviewed the practical problems in using the multi-hit model. In general, the multi-hit model does not appear to be viewed favorably as the primary basis of cancer risk extrapolation.

Multistage model--The multistage model, first proposed in 1953 and described by Armitage and Doll (1961), after whom it is often named, is based on considerations similar to those of the multi-hit model. This model assumes that cancer begins in a single cell (or cell line), but only after it has undergone a number of random biological events or stages. (Note: in the multi-hit the events must occur in some nonrandom sequence.) The stages are independent; the time spent in each stage is exponentially distributed; the effects at some stages are additive with background effects; and the age-specific rate of occurrence of each event is linearly related to dose. The multistage was not derived on the basis of stages of initiation, promotion, etc., as now identified, did not consider the possibility of repair mechanism or tumor regression and did not distinguish between benign and malignant tumors.

The generalized multistage model, as developed by Crump et al. (1976, 1977), Guess and Crump (1976, 1978), and Guess et al. (1977), assumes that background carcinogenesis is present, and that exposure to a new carcinogen acts additively. The probability of response, P(d) from continuous lifetime exposure at dose, d, is given by the equation:

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* A version in which background is additive is essentially equivalent to the multistage model.

$$P(d) = 1 - e^{-(\beta_0 + B_1 d + \beta_2 d^2 + \dots \beta_k d^k)}$$

where k = an integer, nominally the number of stages in the process, and

β_n = nonnegative parameters to be estimated from the data set.

The equation is obtained in essence* by replacing the single parameter of the one-hit model by a polynomial; the one-hit is a special case obtained by setting k = 1. If the background incidence is zero, then $\beta_0 = 0$ and the equation at low dose is:

$$P(d) = 1 - e^{-(\beta_1 d + \beta_2 d^2 + \dots \beta_k d^k)}$$

A threshold version of the multistage can also be obtained by replacing d with $d-d_t$, where d_t is the threshold dose.

$$P(d) = 1 - e^{-[\beta_0 + \beta_1(d-d_t) + \beta_2(d-d_t{}^2) + \dots \beta_k(d-d_t)^k]}$$

Numerous publications in the late 1970's supported the multistage models' biological and statistical bases, demonstrated how maximum likelihood estimates of risk could be calculated and described methods of using confidence limits to estimate virtually safe doses (VSDs). See: Crump et al., 1976, 1977; Guess and Crump, 1976, 1978; Guess et al., 1977; Hartley and Sielken, 1977; NRC/NAS, 1977a; Brown, 1978; Guess and Crump, 1978; Peto, 1978; Crump and Masterman, 1979; and Crump, 1979. Of particular interest were arguments basing a demand for low dose linearity on the assumed additivity of response from the administered dose and a postulated effective background dose. A further development was the use of upper 95% confidence limits to give more stable estimates of risk above background than were obtained for MLEs. The low-dose linearity hypothesis** was justified both on the basis of background additivity and by reference to the then-held BEIR committee view on radiation and cancer (NRC/NAS, 1972).

The multistage model is very flexible in fitting data sets because of the polynomial function of dose. In fact, the general model is so flexible that it does not yield just a single solution when fitted to a data set; several solutions can be obtained, the number depending on the number of terms used in the polynominal. Different solutions, however, can give substantially different estimates of risk at very low doses, and thus a high degree of uncertainty in extrapolated risks (Carlborg, 1981b). In order to avoid this problem, the number of terms permitted is arbitrarily limited* to the number of nonzero dose levels in the data set. This convention slightly weakens the biological basis of the model; the number of stages of cancer for a given carcinogen is nominally dictated by the experimental design. (For some data sets, only two or three parameters are needed to achieve a satisfactory fit). In addition, the linear hypothesis is satisfied only if $\beta_1 > 0$. Therefore, an arbitrary decision is usually made that a positive β_1 parameter must be included in the regression analysis, although satisfactory fits can be obtained at times without it (Guess and Crump, 1978). Because of these conventions, however, a possibility usually remains that a better-fitting solution was unidentified--one that would have given a different estimate of low-dose risk for regulatory considerations.

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* The multistage model also can be derived from the probit model (Altshuler, 1981).

** The "hypothesis" has been termed a dogma by some (Hartley and Sielken, 1977).

Carlborg has evaluated the multistage model on the basis of theory and experimental results, and discussed several "defects" in the application as a model for carcinogenesis (Carlborg, 1981b). Sielken (1985c) found that for formaldehyde carcinoma data, a five-stage multistage model gave a much better fit to the data than did a three-stage version with the conventional restrictions (see above), and also gave substantially lower estimates of risk at low doses (being similar to those of the Weibull model). In contrast, the 95% upper confidence limit of the five-stage model at low dose was substantially higher than that limit for the Weibull because of differences in the model families and their upper confidence limit procedures. Interestingly enough, the 95% lower confidence limit curve for the five-stage model fell so far below the maximum likelihood estimate that it indicated the possibility of quite negative risks at low doses. This effect was minimal with the Weibull.

Crump et al., describe a regression procedure for computing the maximum likelihood polynomial function from a data set. Referred to as a "global maximization" procedure, it can be performed efficiently with the computer program GLOBAL (Crump et al., 1977; Crump and Watson, 1980; Crump, 1981b), accessible through the National Institutes of Health, Bethesda, MD. Whenever the multistage model does not fit the data sufficiently well, data at the highest dose are deleted, and the model is refitted to the rest of the data. This is continued until an acceptable fit to the data is obtained (i.e., the chi-square statistic). GLOBAL also readily computes the extra risk over background, confidence limits on the risk, and the virtually safe doses at specified low risks.

Despite its flexibility, the conventional multistage model does not give a satisfactory fit to data sets in which the dose-response function rises steeply, then plateaus (i.e., strongly concave).** In addition, a few data sets are known for which the fitted multistage curve is concave at moderate to low doses.*** In extrapolation to very low dose, the multistage model and its upper confidence limit become essentially linear. With most adequate monotonic data sets it gives estimated risks higher than those of the probit, logit, multi-hit, and Weibull models, and often nearly as high as those of the one-hit model.

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* The βs are also constrained to nonnegative values so that only monotonic relationships result.

** Chemicals giving such data sets include DDT, DES, ethylene dibromide, and vinyl chloride (Carlborg, 1981b).

***Examples include 2-AAF, NTA, and hexachlorobenzene (Krewski and Van Ryzin, 1981).

Gibb and Chen (1986) recently proposed a variation of the multistage model that could address multiplicative carcinogenic effects as well as the conventionally assumed additive effects.

Linearized multistage model--In the "linearized" multistage model (Crump, 1981a, 1981b), the linear term (β_1) in the polynomial function is replaced by its upper 95% confidence limit, q*, and the nonlinear terms d^2,d^3 etc., are dropped entirely (because at low dose they approach zero faster than d does). The best estimates of β_1, β_2, β_3 etc., are never used in the linearized version.

Crump and Watson (1980) calculated the upper 95% confidence limits of risk by both the linearized multistage model and the one-hit model for 90 sets of data, and compared then for purposes of developing water quality criteria. The models coincided for the 16 sets having only two dose groups, gave identical fits and extrapolated risks for 28 sets, gave negligible differences for 28 other sets. The multistage gave risks 1/2 as large in 17 sets, and gave risks less than one-fifth as large in one case. That the multistage model gave upper confidence limit risk estimates in such good agreement with those by EPA's then-approved one-hit model was persuasive. That it also had a better biological basis in many opinions, gave a better fit to experimental data, and avoided some of the excessive conservatism of the oft-criticized one-hit model, was irresistible. EPA substituted the linearized multistage model for the one-hit model in its water quality criteria (EPA, 1980a), and subsequently described this method as the basis of its cancer risk assessments (Anderson et al., 1983; EPA, 1986a).

In the linearized multistage model, the "extra" risk* R(d) above background incidence $P(d_o)$ at dose d is defined (as in Subsection B.2.a.1) as:

$$R(d) = \frac{P(d) - P(d_o)}{1 - P(d_o)}$$

Computation for the linearized multistage model are made using the GLOBAL program of Crump and Watson (1979) as updated. The multistage model is first fitted to the data, using a number of terms i the polynomial equal to the number of dosed groups in the study beside the control group. The fit of the model to the data can be tested if desired by the chi-square statistic.

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* The symbol used for this extra risk varies among EPA documents and also among literature publications, with A(d), $P_t(d)$ and others in use.

$$\chi^2 = \sum_{i=1}^{b} \frac{(x_i - N_iP_i)^2}{N_iP_i(1 - P_i)}$$

where N_i is the number of animals in the i^{th} dose group, x_i is the number of animals in the i^{th} dose group with a tumor response, P_i is the probability of a response in the i^{th} dose group estimated by fitting the multistage model to the data, and h is the number of remaining groups. The fit is determined to be unacceptable whenever χ^2 is larger than the cumulative 99% point of the chi-square distribution with f degrees of freedom, where f equals the number of dose groups minus the number of nonzero multistage coefficients. If the fit is unacceptable, data at the highest dose are deleted and the model is refitted to the rest of the data. This is continued until an acceptable fit to the data is obtained. A fit will always be obtained for the lowest dosed group, even if the response appears anomalously high compared to higher dosed groups.

The upper 95% confidence limit of the best estimate, q_1 value is calculated by remaximizing the log-likelihood function (L_1) for q_1. The value of q_1 is increased to a value q_1^* such that the maximum value of the log likelihood function L_1 satisfies the equation:

$$2(L_0 = L_1) = 2.70554$$

where 2.70554 is the cumulative 90% point of the chi-square distribution with one degree of freedom, which corresponds to a one-sided 95% upper limit.

At very low doses the upper confidence limit on the extra risk is always linear with the linearized model, and q_1^* will always be positive. The extra risk is then essentially equal to the product of q_1^* and dose: $R(d) \sim q_1^*d$. The lower 95% confidence limit on the dose producing a given risk can be calculated from the upper 95% value for q_1^*. A "virtually safe dose" can be defined as the dose for which the extra risk is not more than some predetermined small number.

$$R(d) = 10^{-5} \text{ or } 10^{-6}$$

The q_1^* values obtained from animal studies must be converted to human equivalent values, which EPA's Carcinogen Assessment Group gave the symbol B_h (Anderson et al., 1983). The interspecies conversion is made on the basis of surface area ratios (as discussed in Section A) using the approximate formula

$$B_h = q_1^* \cdot \left(\frac{70}{W_a}\right)^{1/3}$$

where W_a is the weight of the test animal in kilograms. CAG has variously called B_h the "upper bound slope," "upper bound potency," the "potency" and "potency factor" of the carcinogen. The converted q_1^* are written as q_h^* in some EPA publications but not in others, and q_1^* is sometimes used for the converted values also. CAG has published values for B_h and VSDs for over 50 carcinogens (Anderson et al., 1983; EPA, 1984d). In addition, CAG has developed a "potency index" for these carcinogens by multiplying the molecular weight of each by its B_h, and also an "order of magnitude index" by taking the logarithm (base 10) of the potency index and rounding to the nearest whole number (EPA, 1984d).

Note that the confidence limits in the linearized multistage are statistically correct only if the model used to compute the limits is an accurate representation of the underlying dose-response function; they do not provide any measure of the extent to which the model is correct or incorrect. In fact, the use of the upper confidence limit in the multistage model can result in a nonzero estimate of risk for data sets that do not show carcinogenicity (Whittemore, 1980).* The Chairman of EPA's Carcinogen Assessment Group recently noted that, overall, a feeling exists that the biological foundation is flimsy for EPA's current method of low level risk estimation based on the linearized multistage model (Albert, 1986).

Weibull model: The Weibull model has been widely used in its time to tumor form (see below), but because of uncertainty over its physiological basis, it was not seriously considered until recently for extrapolation of risks to low dose. It was first proposed in 1951 by Fisher and Holloman (Brown, 1985) on the basis of a mechanistic multicellular theory of cancer: a tumor arises from a clone of cells, each of which has undergone a single cellular change. In 1966, Pike suggested the Weibull distribution for analysis of carcinogenesis experiments involving continuous exposures, and in 1971 Doll considered its implications as a model for carcinogenesis. The model adequately described the observed age distribution of many mice and human cancers, according to Peto and Lee (1973), who improved procedures for estimating the parameters of the model.

A familiar time-independent form of the Weibull model** is expressed by the equation

$$P(d) = 1 - e^{-(\alpha + \beta d^m)}$$

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* A useful measure of the uncertainty of low dose estimates might be obtained by calculating best estimates and upper and lower confidence limits with two or more reasonable models.

** A general form of the Weibull distribution is:

$$P(t,d) = 1 - e^{-(\alpha + \beta d^m)(t - w)^{k-1}}$$

where t is the time after dosing starts, w is tumor growth time, and k is a number of discrete changes leading to tumors.

where P(d) is the probability of response at dose d and α, β, m are parameters to be estimated ($\beta, m > 0$). Alpha (α) is determined by the background tumor incidence; β, a scale parameter, depends on the units of dose; m, a shape parameter, is usually in the range 1 to 5 (not necessarily an integer), although a few data sets are known with m of 0.5 or less. Alternatively,

$$P(d) = 1 = e^{-\beta d^{m}}$$

if the background incidence is negligible ($\alpha \simeq 0$) or if one wishes to express the extra probability over background. The relationship at the low end of the dose range is linear if $m = 1$, convex (sublinear) if $m > 1$, and concave (supralinear) if $m < 1$, as in a few cases where the curve rises rapidly and then plateaus.* At very low doses, the extra risk over background is $R(d) \simeq \beta d^{m}$. The virtually safe dose (VSD) corresponding to a one in a million risk over background is given by:

$$VSD = \left(\frac{10^{-6}}{\beta}\right)^{1/m}$$

When $m = 1$, the VSD would be the same as that calculated by the one-hit model.

The Weibull thus contains the low dose form of the one-hit model as a special case, and is sometimes described as a generalization of it (Van Ryzin, 1980). The Weibull can also be derived as a variation of both the multistage and multihit models (Crump, 1985a). Christensen and Chen (1985) have suggested a mechanistic-probabilistic basis for the Weibull model. Hence, it is better classified with the mechanistic models (Brown, 1985) than with the tolerance distribution models, as it sometimes is (Munro and Krewski, 1981; Krewski and Van Ryzin, 1981; Park and Snee, 1984; Morriss et al., 1984).**

The Weibull model is very flexible and easily fitted to most data sets. A linear weighted least squares regression program can be used with just a small calculator in a trial and error method to determine the three parameters in the Weibull model. One such program which handles up to nine data points was made available by the Food Safety Council in 1980. Nonlinear weighted least squares regression computer programs were also in use at that time to estimate the parameters directly, and a nonlinear maximum likelihood method program was available from Krewski at the Directorate of Health and Welfare, Canada (Food Safety Council, 1980). Similar programs have been developed by Crump and Howe and perhaps by others (Crump and Howe, 1985).

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* Supralinear behavior appears to be observed most often when the chemical has low acute toxicity or a substantial difference exists between administered dose and effective dose because of metabolic or behavioral effects. Examples are DDT, trichloroethylene, and vinyl chloride (Carlborg, 1981a; EPA, 1985a).

** The Weibull is sometimes termed the Weibull Multihit Model (Van Ryzin, 1980) and also the Extreme Value Model (Krewski and Van Ryzin, 1981; Rowe et al., 1983) because of similarities to the extreme value distribution, i.e., $F(x) = 1 - e^{-e^{x}}$.

Because the exponent of the dose (m) is allowed to take fractional values (rather than being constrained to integers as in the multistate), an excellent fit can usually be obtained if the observed data exhibit a conventional spread and shape. The standard form of the Weibull generally can give a good fit to data that exhibit threshold-like appearance (e.g., the ED_{01} bladder data), or it can be modified to accommodate a threshold dose. Overall, in curve fitting the Weibull combines the better features of mechanistic models such as the multistage and multihit with those of the tolerance distribution models such as the probit and logit.

Carlborg (1981a) applied the Weibull model to 31 cancer data sets for 15 chemicals (plus a study in which protein and caloric intakes were varied).* He reported generally satisfactory fits for the Weibull to these data (27 sets), and noted that none yielded a best fit corresponding to the one-hit special case (i.e., $m \simeq 1.0$). The Food Safety Council (1980) and Krewski and Van Ryzin (1981) compared the fit and low dose extrapolation properties of several models (including the Weibull) to data sets for 14 substances, the response being cancer in nine cases and other than cancer in five cases. The multihit, multistage, and Weibull models all gave fits consistently superior to that of the one-hit model, which frequently gave quite inadequate fits. The multistage model, as usually constrained, did not give quite as good a fit in general as the multihit or Weibull, the Weibull being the choice of displaying the data graphically. Carlborg (1981c) tested three versions of the Weibull model (varying dose, time to tumor, and duration of exposure) against data from the ED_{01} study and found good fits in all cases for both liver and bladder tumors. Christensen (1984) found the Weibull to have considerable promise in analysis of aquatic toxicology, and Christensen and Chen (1985) have found it promising in predicting the combined toxicity of two or more chemicals.

The low-dose extrapolation characteristics of the Weibull are generally similar to those of the multihit model. The extrapolation is nearly linear, and the risks calculated at very low dose are usually lower than those of the multistage model and near the middle of those for all the common models (Krewski and Van Ryzin, 1981). For a few data sets, however, the Weibull gave higher estimates of risk than the multistage model, although not as high as the one-hit model (EPA, 1985a). Extrapolated risks with the Weibull appear to be more sensitive to low dose data points than those extrapolated by the multistage (EPA, 1985a; Brown, 1985).

Van Ryzin and Rai (1987) introduced a variation of the Weibull model which incorporates the concept of the effective dose. The administered dose is transformed by Michaelis-Mentor nonlinear kinetics to give an equation with four parameters,

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* Carlborg (1981a) used the computer program BMDP3R for curve-fitting.

$$P(d;\theta) = 1 - e^{-\left[\theta_1 + \theta_2 \left(\frac{d}{1 + \theta_4 d)}\right)^{\theta_3}\right]}$$

where d is the administered dose, and θ_1, θ_2, and θ_3 are all > 0. θ_1 and θ_3 are the same, respectively, as the α and m in the Weibull* and θ_2 is a product of the Weibull β and a constant raised to the m power. Substituting these gives the form

$$P(d) = 1 - e^{-\left[\alpha + \beta a_1{}^m \left(\frac{d}{1 + a_2 d}\right)^m\right]}$$

where a_1 and a_2 are constants related to the maximum rate of change and the Michaelis-Mentor constant, with $a_2 > -1/M$, where M is the maximum dose administered in a study. A one-hit version of the model results if $\theta_3 = 1$ and $\theta_4 = 0$, and variants of the multihit and multistage models result if θ_3 is a positive integer > 1. The authors applied the one-hit version of their nonlinear kinetics model to data sets for vinyl chloride, DDT, and saccharin which showed concave, linear, and convex dose-response curves, respectively. The fit was better than for the conventional one-hit, and the model was judged to be "reasonably adequate" for these three carcinogens. The model gave a virtually safe dose for saccharin intermediate between those calculated by the conventional one-hit and Weibull models. These authors did not apply the kinetics-adjusted Weibull to these data sets.

As noted in the opening paragraph, reservations about the biological basis of the Weibull model for cancer (i.e., the multicellular hypothesis) has limited its application in low dose extrapolation of risks. Because of its other desirable features, strong interest has developed recently in reevaluating its foundations. Carlborg (1981a, 1981b) has noted in fitting the Weibull to 27 data sets that the shape parameter, m, tends to have values that can be expressed as a fraction, I/2, where I is an odd positive integer, i.e., m typically has such values as 1/2, 3/2, 7/2, etc. The physiological implications of this observations are uncertain, but toxicokinetic factors may be involved. In addition, Carlborg (1981a, 1981b) notes that the extended (time-to-tumor) Weibull model can be used directly to derive a 1967 empirical observation by Druckrey that the dose multiplied by the median time-to-tumor raised to a power is a constant,** i.e.,

$$d \times t^n = \text{constant}$$

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* θ_3 governs the shape of the curve in the low dose range in the same way as m in the Weibull.

** Recent results indicate that Druckrey's rule holds for genotoxic carcinogens, such as N-nitrosamines, but not for the nongenotoxic carcinogens, Dieldrin, a chlorinated pesticide (Pereira, 1985).

Carlborg also noted that the extended multistage model could not be used in the general case to derive Druckrey's rule.

Christensen and Chen (1985) recently found that certain mechanistic assumptions about the reaction of toxicant molecules with key receptors of the organism and probabilistic assumptions regarding the concentration of blocked receptors at any time led directly to the Weibull model. The shape parameter, m, can be interpreted as the average number of toxicant molecules per receptor. These authors suggested their conceptual model particularly for cases where response occurred mainly in a single organ site in the organism (i.e., sites with vulnerable key receptors), and concluded that the parameters of the Weibull model are not simple results of fitting a curve to data, but have chemical-toxicological significance.

Alternative biological rationales occur to the present author that may provide an improved theoretical basis for applying this model to low dose cancer extrapolation. For example, in place of the multicellular hypothesis, the Weibull may be applicable to multiple events within a cell, such as attacks by the carcinogen molecules on multiple chromosomes, on multiple genes, on multiple nucleotides along a DNA strand, or on multiple parts of a cell (including membranes). The Weibull distribution may be applicable to situations where multiple agents interact in the same (or nearby) cells to cause cancer--the agents possibly including carcinogens naturally occurring in foods, trace environmental contaminants, natural radiation products, and viruses, in addition to the test carcinogen. Many carcinogens are known to form adducts with DNA, the strength of the adduct reflecting the potency. Binding occurs at four sites primarily (guanine, cytosine, adenine, and thymine), but different carcinogens prefer different sites. Such considerations may fit comfortably into a Weibull model, together with other interactions such as multiple enzyme effects and cell killing.

Time-to-effect models: Because of the latency periods observed for cancer, the time-to-appearance of tumors may be an important consideration in developing regulations for carcinogens. The original versions of several of the common dose-extrapolation models incorporated time-to-effect as well as dose. These include variations of the probit (log-normal and log-time), log-logistic, gamma multihit, multistage, and Weibull, and also others such as the general product, Hartley-Sielken and Daffer-Crump-Masterman models (Daffer et al., 1980; Krewski et al, 1983; Crump and Howe, 1984; Crump, 1985b; Bickis and Krewski, 1985; and Sielken, 1985). One example of an equation for such a model is shown below for one form of the Weibull model:

$$P(d,t) = 1 - e^{-\beta d^{m} t^{k}}$$

where t = time (e.g., age),

k = parameter to be estimated, and

β, m = parameters to be estimated as in the time-independent Weibull

This model was found to fit very well the data from the ED_{01} study (Kodell et al., 1980), as did a variation that included a factor for duration of exposure (Carlborg, 1981c). Van Ryzin (1981) found that the two-parameter form of the Weibull with time-to-tumor did not fit the ED_{01} data as well as did the Hartley-Sielken model (nor did the one-hit or extreme value models). Salzburg (1981) reported good fit of the three-parameter Weibull to the ED_{01} bladder data and for a modified Weibull to the liver data.

The Moolgavkar-Venzon-Knudson (MVK) two-stage mathematical model (Moolgavkar and Venzon, 1979; Moolgavkar and Knudson, 1981) is well regarded for cancer risk assessment. It has a biological basis in cellular dynamics and transformations and incorporation of time-to-tumor. The equation has the form

$$I(t) = \mu_1 \mu_2 \int_0^t X(s) e^{[(\alpha_2 - \beta_2)(t-s)]} ds$$

where I(t) is the cancer incidence at time t, X(s) is the number of susceptible cells at any time (assumed to be deterministic and known), μ_1 and μ_2 are rates of cell change in reaching the first event and full malignancy, respectively, and α and β are cell formation and death rates, respectively.

Thorslund et al. (1987) and Chen et al. (1988) have proposed dose- and time-dependent and age-specific cancer risk functions based on the MVK model. Moolgavkar and Dewanji (1988) caution that the derivation of Thorslund et al. contains an approximation that may be adequate for human cancer incidence rates, but is unlikely to be valid for animal experiments with very high tumor rates.

Sielken (1987) has described an Individualized Response Model (IRM) that incorporates much of the available physiological and pharmacological information on cancer and is an extension of the MVK two-stage model. Sielken, Inc., of Bryan, Texas, offers a computer program, GEN.T (operable on IBM-compatible personal computers with math coprocessors) for using the IRM.

While some authorities believe that time-to-effect models should receive high priority in regulatory deliberations, others have doubted that they will be of significant value in the near term because so few studies described in the literature to date have obtained these data.

(5) Evaluation of dose-response extrapolation models: The merits of the various models for low dose extrapolations of quantal data have been extensively discussed. Questions remain about which if any should be used as a basis for regulatory decisions, particularly for carcinogens (Krewski and Van Ryzin, 1981; Clayson et al., 1983; Crump, 1985a, 1985b; and OSTP, 1985). The Environmental Protection Agency and its Carcinogen Assessment Group have stated that no single mathematical model is recognized as the most appropriate for low-dose extrapolation (EPA, 1986a; Anderson et al., 1983), as also has the Office of Science and Technology Policy (OSTP, 1985).

A major problem is that the uncertainty increases as one moves away from the experimental dosage range to lower and lower doses in the extrapolations. The problem is suggested schematically in Figure VIII-4. The divergence arises from uncertainty over whether the model is applicable at very low doses, and also from statistical uncertainty in applying a model to a particular data set. The most likely estimate at very low doses becomes increasingly unstable with a small change in the response at experimental doses. The use of the upper confidence limits for the multistage or linearized multistage reduces the instability problem in estimating maximum risks and virtually safe doses. One must keep in mind, however, that this is a model-based confidence limit. The upper and lower confidence limits of risk are those bounded by a straight line extrapolation from the lowest data point (or its toxicology-based statistical upper limit) to the background level and by a threshold dose.

A second problem, as already indicated, is that the several models (none of which are based on biochemical mechanisms of toxicity) estimated substantially different risks at low doses. Figure VIII-5 (adapted from Munro and Krewski, 1981a, 1981b) illustrates the range one usually gets when the common models are used to extrapolate data for carcinogens. Suggestions have be made (see, for example, Food Safety Council, 1980) that extrapolations be made with more than one of the flexible models, and that the resulting estimates of virtually safe doses be considered in decision making.

A third problem is that while computer programs have been developed to fit most of the various models to data sets and to make extrapolations, scatter in the original data can prevent attaining a satisfactory fit (e.g., chi square statistic test). In this case, the standard procedure is to drop the data point at highest dose and reattempt the fit. If fit is still unsatisfactory, the next highest dose point is dropped and so on until a fit is achieved. For data with much low end scatter, this procedure can result in discarding midrange data points that should be the most reliable, and in the worst case, one could end up with only the lowest, usually least reliable point.*

A fourth problem is that many of the data in the literature for toxic substances (including a great many of those frequently found in hazardous wastes) were developed at a time when toxicological standards were less demanding. Not uncommonly, only two dose groups plus a control group were studied in animal tests. For carbon tetrachloride, a major industrial chemical for many decades, the best available dose-response data for carcinogenicity shows two dose groups; the highest dose gave 96.5% response, the low dose 100%, and the controls (7.7%) (NCI, 1977).** The flexible multistage

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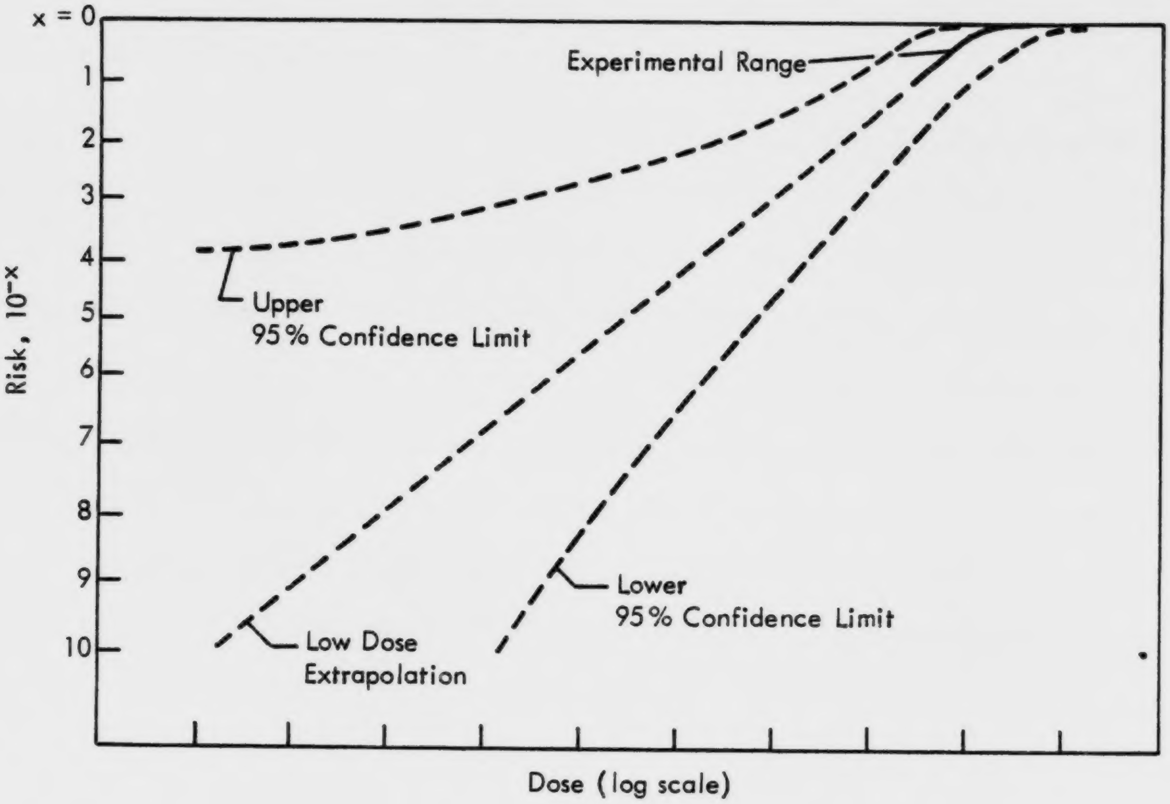
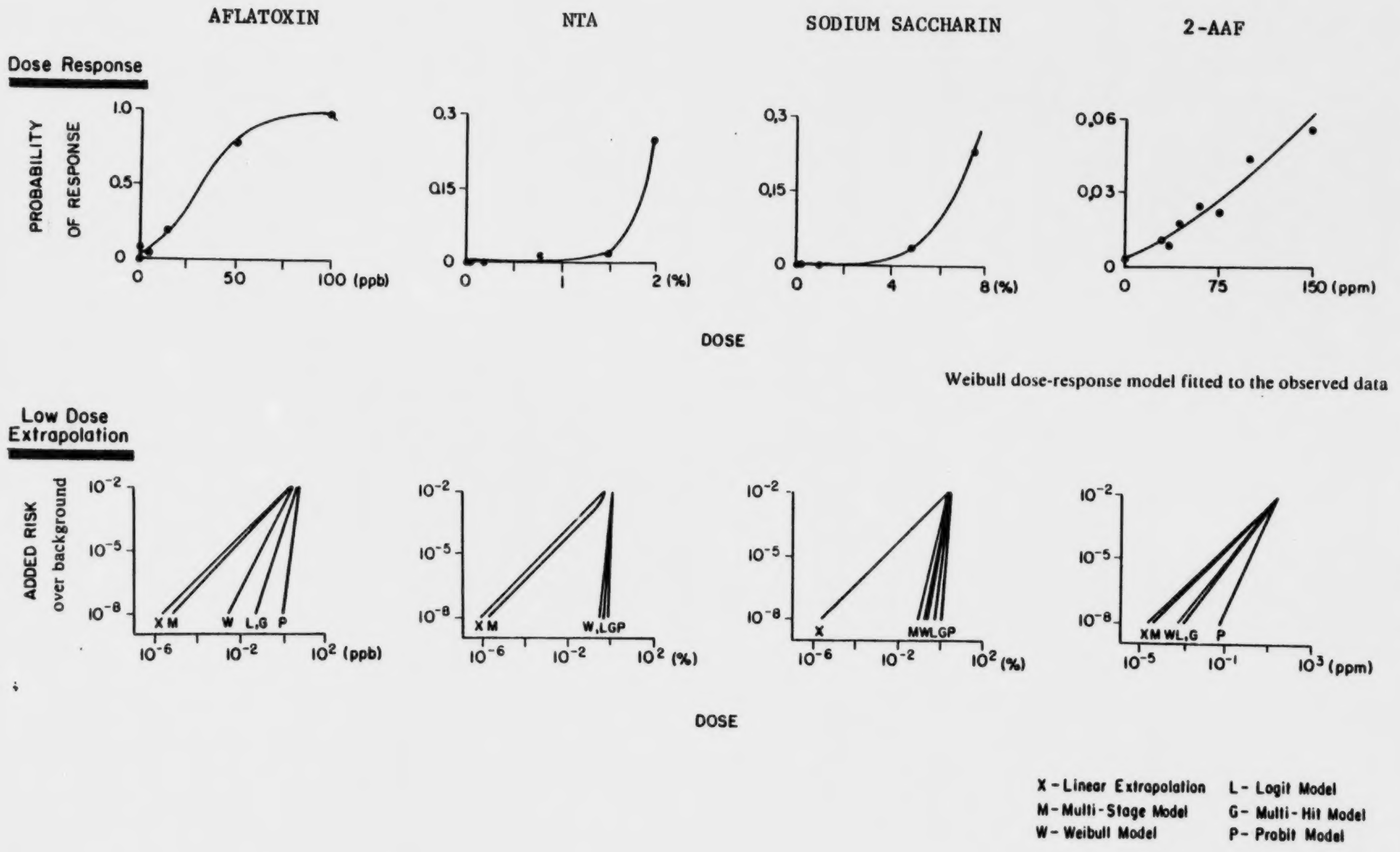
* Interestingly enough, Brown (1985) found that for the good data sets for bladder and liver cancer in the ED_{01} study, dropping the lowest data points had negligible effect on the extrapolated VSDs (10^{-6} risk) by either the multistage or probit models. The effect on the best estimates was not reported.

** This example is atypical of NCI test results. In fact, 100% cancer response at tolerated doses is unusual.



Source: Lawless (1986).

Figure VIII-4 - Illustrative Increase in Uncertainty for Low-Dose Extrapolation



Source: Adapted from Munro and Krewski, 1981b.

Figure VIII-5 - Dose-Response Data and Low Dose Extrapolations with Various Models for Four Carcinogens

model can be easily fit to the data, but the systematic uncertainty at low dose extrapolation is inherently very high.

In summary, mathematical models have been used extensively for estimating cancer risks at low doses; they have been used (either in the form of maximum likelihood estimates, upper 95% confidence limits, or VSD estimates) for regulatory purposes. Mathematical models have sufficiently serious problems, however, that several alternatives to the use of a single model have been suggested. Some authorities suggested extrapolation along a fitted model to, say, a 1% risk, and then linear extrapolation at lower doses. Others suggested 10^{-2} to 10^{-4} risk as the switch point (Van Ryzin, 1980). Other authorities have endorsed reporting some combination of best judgment point estimates and maximum plausible risk estimate or best estimates with both upper and lower confidence limits (Park and Snee, 1984), and still others have suggested taking into account the best estimates calculated by three or four models (Food Safety Council, 1980).

If mathematical extrapolation is used, the model(s) selected should meet at least three criteria: (1) it should be capable of fitting observed dose-response data for a wide range of chemicals if it is expected to have much credibility in extrapolations below the observed dose range; (2) it should be in agreement with (or at least not in disagreement with) our understanding of the mechanisms of carcinogenesis; and (3) it should be useful with the kind of data sets likely to be available for chemicals typically found in hazardous wastes. These criteria appear to rule out use of the Mantel-Bryan and one-hit models. The models of choice seem clearly to be the multistage and the Weibull. Both have good flexibility in being fit to diverse data sets, and usually become essentially linear in low dose extrapolation. The multistage has been well regarded because of its rationale, utility, and "conservativeness." Its linearized version gives linear upper confidence limits on risk in extrapolation. On the other hand, opinions have been expressed that the multistage models estimate risks that are too high at low dose to serve as the primary basis of regulation (particularly when substantiating observations on humans are lacking). The fact that the linearized multistage model gives nearly the same estimates of low dose risk as the discarded one-hit model is a cause of substantial concern. The Weibull model has become increasingly well-regarded of late both on theoretical and practical grounds. It usually gives estimates of risk near the middle of those for all of the common models (i.e., usually lower than that of the multistage). On this basis, the Weibull could be considered useful in making best estimates of low dose risk to complement confidence limit estimates by the linearized multistage and a threshold model.

c. Toxicokinetic (pharmacokinetic) models: From a biological viewpoint, toxicokinetic* models are the best models, although their use has substantial limitations. This class of models embodies more basic and comprehensive concepts than the fixed mathematical models discussed in the preceding subsections.

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* Pharmacokinetics, a term introduced in the pharmaceutical literature, is often used also in chemical risk assessment, but toxicokinetics is the broader term. In disciplinary classifications, toxicology is placed in the biological sciences and pharmacology in the medical and health services field.

Cornfield (1977) noted that the probit and logit models generally gave similar results to toxicokinetic models in the 5 to 95% response range, and developed a method of estimating parameters, particularly the doses saturating metabolic mechanisms. Ramsey and Gehring (1981) described methods for applying pharmacokinetic principles to improve risk assessments and noted particularly the need to estimate the retained dose in animal subjects and exposed humans. Withey (1985) recently reviewed the pharmacokinetic differences between species, and Hoel (1985) reviewed the incorporation of pharmacokinetics into low-dose extrapolations. Papers in Woodhead et al. (1985) discuss many biological mechanisms and extrapolations. Chandler (1985) has compared biochemical mechanistic models with other models proposed for quantitative risk assessment, and urged greater use of the former.

Toxicokinetic models require a good deal of information about the absorption, distribution, storage, metabolism, and excretion of a chemical in the organism, including the concentration of the chemical or its toxic metabolites as a function of time in the various body compartments relevant to the effect produced (e.g., concentration in the blood, liver, bile, adipose tissues, urine, and the target organ). This information is analyzed mathematically in a series of kinetic equations (first order kinetics usually can be assumed), and then an appropriate mathematical expression is developed for the dose-response function in the test species.

Accurate extrapolations across exposure routes usually can be made with these models, and they can be combined with other models for low-dose extrapolations. Accurate extrapolations across species can be made with toxicokinetic models if sufficient data are available for any critical differences (e.g., metabolism, pathways and rates) for the second species. Unfortunately, the use of toxicokinetic models is severely limited by the lack of data. In particular, most data on humans have been collected on chemicals of pharmaceutical interest rather than on environmental contaminants.

d. Other predictive methods: Several other approaches are available to help predict the kind and degree of adverse health effects of a chemical. In general, these methods would be most useful when the available toxicity data base is inadequate to permit use of a toxicokinetic model or one of the better low dose extrapolation methods described above. These approaches vary substantially in qualitative and quantitative characteristics, and in the uncertainty of the results they yield. They could be useful in some cases (possibly in combination with each other and with low-dose extrapolation methods) in assessing risks of hazardous waste disposal, and are therefore summarized below. Approaches included are: Potency indices; extrapolation from nonchronic data; comparison with cognate chemicals; use of short-term microbiological and biochemical tests; use of ADIs and TLVs; and nonparametric methods.

(1) Potency indices: Several authorities have suggested that an index of cancer potency, based on dose-response results in the experimental range, should be used as a basis of regulation in place of any of the proposed mathematical models for extrapolating risks to very low doses. Several approaches to developing such indices have been proposed, some of which incorporate mathematical treatments. See for example: Meselson and Russel (1977); Crouch and Wilson (1979, 1982); NRC (1980d); Squire (1981); OTA (1981); Clayson et al. (1983); and Park and Snee (1984).

An approach by Peto et al. (1984) is of particular interest because of its simplicity, and because a data base of potencies developed with it for 770 compounds tested in 2,944 chronic animal bioassays was published concurrently and subsequently by Gold et al. (1984; 1986). Their index, the tumorigenic dose rate or TD_{50} is analogous to the LD_{50} for acute toxic effects. The TD_{50} (in mg/kg/day) is the administered dose giving 50% increase in tumors in the test subjects over a standard lifetime of exposure. Gaylor and Chen (1986) used this data base to compare relative carcinogenic potencies in the most commonly used test animals. Mean ratios of mean minimum TD_{50}s for rats:mice were 1:1.22 and 1:1.13 by diet and gavage, respectively, and 1:1.48 for liver tumors by diet. Minimum TD_{50}s were generally still higher for hamsters than for mice, but generally within a factor of 100 for all three rodents.

Inhalation data gave the poorest agreement between rats and mice. Ames et al. (1986) used TD_{50}s to compare and rank the possible hazards of 36 naturally occurring and man-made carcinogens to which humans are exposed almost daily. The ranking suggested that the natural substances could be of greater carcinogenic hazard than such environmental contaminants as pesticide residues or water pollutants. Portier and Hoel (1987) discussed several potential sources of error in estimating TD_{50}s, and suggest that use of tumor incidence rate instead of tumor death rate would impact this potency index.

EPA's Carcinogen Assessment Group developed a quite different approach to potency indices, as reported in recent issues of the series of health assessment documents on specific chemicals, published by the Office of Health and Environmental Assessment (e.g., EPA, 1984c). CAG's potency is based on a mathematical extrapolation rather than directly on the observed data. The slope of the upper confidence limit is first calculated by applying the linearized multistage model to the data, as described by Anderson et al. (1983). The slope is then multiplied by the molecular weight of the chemical to compute the potency index, which can be reported either directly or as an order of magnitude index. For many applications, the slope value may be of greater use directly than the index.

CAG has also published upper bound "unit risk" estimates for a number of air pollutants of concern to EPA, where the unit risk is defined as excess lifetime risk for a 70 kg person from breathing 1 $\mu g/m^3$ of the chemical over a 70 year lifetime (Anderson et al., 1983). The model used to obtain these indices of carcinogenic potency was not stated in the publication but was either the one-hit or linearized multistage.

While potency indices in general can be valuable in comparing the relative carcinogenicities of a large number of chemicals, they have not been shown to date to be helpful in predicting response at very low environmental exposures for a given chemical. They do not appear to be sufficiently developed at present to be useful as dose-response functions in predicting the number of cases of adverse effects in a given population at a predicted environmental exposure. They could be useful, however, in some comparative risk assessments wherein the alternative waste disposal technologies produced different carcinogens. Potency indices have not been used to date for regulatory purposes, and it appears unlikely they will be until a definition has been accepted for a "safe" index for some standard reference carcinogen.

(2) Extrapolations from nonchronic or other data: The response of an organism to a chemical at one level of exposure sometimes can be inferred from epidemiological or animal data at another level of exposure. The uncertainty will vary with the nature of the chemical and the response.

In some cases the nature of the responses may be similar, and information on metabolism, accumulation, etc., can be considered in extrapolating effects between different intensities and durations of exposure. Extrapolation of subchronic exposure data to chronic response will most often be of use in hazardous waste disposal assessment. Dourson and Stara (1983) proposed that chronic NOELS, NOAELS, or LOAELS could be estimated from their subchronic counterparts by dividing by a factor. Related extrapolation methods have been used to estimate upper risk limits of some end points. Alarie (1981) measured the immediate decrease in respiratory rate (a measure of irritation) as a function of dose of inhaled gases and vapors, and calculated the RD_{50} (dose which halved the respiratory rate). Although the RD_{50}s varied by over five orders of magnitude, 3% of the RD_{50} was a good estimator of the TLV for permissible occupational exposure for humans. Similarly, Kenaga (1982) calculated the ratio of acute to chronic toxicity of toxicants for various aquatic species. Acute LC_{50} (median lethal concentration) divided by the maximum acceptable concentration (a chronic NOEL) gave a range of over five orders of magnitude, but most ratios were less than 100 (i.e., exposures of about 1% of the LC_{50} posed a relatively low risk).

In other cases the nature of the response may be different under exposure conditions substantially different from those used in available studies. Prediction of carcinogenic response is particularly difficult, but might be possible. Zeise et al. (1984) found an empirical relationship between the acute toxicities (LD_{50}s) of many chemicals and their carcinogenicities following chronic exposures. Although a biological rationale was not suggested for such a relationship, they proposed that it could be used to make preliminary estimates of the carcinogenic potency of an unstudied chemical, and to give an idea of the uncertainty of the estimate. Such a relationship seems quite reasonable if the chemical kills cells in rough proportion to dose, and if the primary target cells are capable of rapid renewal (i.e., rapid cell proliferation is associated with cancer). In the future, theoretical advances and experimental data bases may permit other correlations of biological effects.*

(3) Comparison with cognate chemicals: The results of chronic tests on cognate (similar) chemicals can sometimes be used to estimate the slope of the dose-response curve, and then comparable subchronic exposure data from the subject and cognate compounds can be used to locate a point on the curve. Standard methods are not yet available, but two approaches have been described: the quantitative structure-activity relationship (QSAR) approach, and the prototype relative potency approach. The literature is still inadequately developed and integrated, but a recent review provides a good bibliography (NRC, 1982).

QSAR approach: If sufficient cognates can be found, QSAR can be used. The basic concept is to calculate regression equations for equi-effective doses of various chemicals as a function of parameters of chemical structure. One then estimates the corresponding dose for the compound of interest. For calculating risks, it is assumed that the dose- response curves of the subject chemical and a well-studied cognate are parallel; the doses of the cognate are adjusted by the ratio of the equi- effective doses (i.e., by relative potency), and effects are calculated. There are two types of QSAR, differing in the kind of structural parameters used for the regression.

The Hansch method, an older and more commonly used approach, is based on physical organic chemistry (Lyman et al., 1982). The parameters may be the usual free energy-related terms (Hammett's σ constant, Taft's steric constant, etc.), newly derived free energy-related terms (such as Hansch's π for lipophilicity), or other parameters that have been suggested (e.g., certain chromatographic R_f's which are proportional to π, some quantum mechanical parameters, or infrared stretching frequencies). Various combinations of the parameters to the first or second power are correlated until one finds the simplest regression equation with a good correlation coefficient. This method requires a close chemical relationship among the toxicants being considered: for instance, Hansch's original study considered the effects of various substitutions on the rings of a series of phenoxyacetic acids on their efficacies as plant growth stimulants.

The Free-Wilson method, a recent development, may be useful in cases where the structural diversity is too great for the Hansch method. In it the regression terms are a series of arbitrary parameters, one per structural feature, having the value one if the feature is present, and zero if it is absent. This method requires (as well as allows) more cognate compounds for equally good suitability of fit. This method has been generalized recently (NRC, 1982).

Prototype relative potency approach: If a sufficient number of cognate compounds with similar biological data are not available in order to prepare a reasonable QSAR, the alternative is to use a method requiring fewer cognates or prototypes, such as the relative potency approach. Using this method, one determines a chemical class or a series of classes each containing the inadequately studied subject chemical and one or more relatively well-studied prototype chemicals for which chronic test data are available. If comparable acute test data are available, one can use the relative potencies of the subject and prototype(s) to estimate the chronic toxicity of the subject chemical.

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* No references were found that suggested that toxicity could be related to odors of chemicals (Van Gemert and Lettenbreijer, 1972; Wright, 1982). Some correlations likely exist, but the subject is complex.

The inherent problems of this approach are that the assumptions are even greater than with QSAR (hence, the uncertainties are greater), and that often the most studied compounds are the most potent; the risk estimates are likely, but not certain, to be too high. The application of this method to risk assessment is very recent and ill defined. One of the few studies of this type has been of synfuels emission products by Health Scientists at Oak Ridge National Laboratory (Dudney et al., 1982; Calle et al., undated).

(4) Short-term microbioassay tests: A wide variety of microbioassay and biochemical tests has been developed and are being used to study certain biological effects. Their common denominators are the use of cultures of mammalian cells, unicellular organisms (bacteria, yeast, etc.), or viruses, usually with *in vitro* techniques. They often use a mutagenic end point, i.e., induction of an inheritable change in the germ plasm of the test specimens. Hollstein et al. (1979) have reviewed the subject. Some of the more common tests are noted below.

The Ames test uses *in vitro* cultures of several mutated strains of *Salmonella typhimurium*, all of which require histidine for growth (Ames et al., 1962, 1973; Maron and Ames, 1983). Aliquots of a bacterial suspension are incubated, in a histidine-deficient medium, with the test chemical; some plates also contain a portion of homogenized rat liver which will metabolize some chemicals in a manner resembling that in the whole animal, so that the mutagenicity of metabolites of the test substance can be studied. The number of observable colonies will be equal to the number of bacteria which revert (mutate back) to the original form, which does not require external histidine.

Many variants of the Ames test are available, particularly the use of different test species. A common variant is the "host-mediated assay" in which a suitable bacterial suspension is incubated in the peritoneal cavity of a mouse or rat, with the toxicant given to the whole animal. Thus, the bacteria are exposed to the toxicant and whatever metabolites are circulating in the blood of the host rodent. Mammalian cells also may be grown in culture, exposed to a toxicant, and examined for mutagenic effects, although determination of an end point may be difficult.

A related procedure is cytogenetics testing, which is usually done on animals already being tested in an ordinary toxicity study. Tissue samples are taken (blood for white cells during the test; bone marrow and kidney at termination) and grown in cell culture. When the cultures are rapidly dividing, the cells are killed and the chromosomes in the nuclei of actively dividing cells are examined microscopically for abnormalities such as breaks, gaps, trisomies (tripled rather than paired), malformations, etc.

Substantial uncertainty is inherent in using short-term microbioassay results to assess human risks to exposure to a chemical. The dose-response relationship may be much different--some linear relationships for mutagenicity _in vitro_ are not _in vivo_ because of the body's defenses--or a mammal may not respond in the same way. In addition, mutagens are not necessarily carcinogens.

(5) _Use of ADIs, TLVs, and RMCLs_: Acceptable exposure levels have been set for many chemicals on the basis of toxicological results and human experience. The U.S. Food and Drug Administration has long established Acceptable Daily Intakes (ADIs) of certain contaminants in foods, drugs, and cosmetics. The American Conference of Governmental Industrial Hygienists and the Occupational Safety and Health Administration have adopted Threshold Limit Values (TLVs) for a large number of chemicals for controlling inhalation exposure in the workplace. The EPA has published Recommended Maximum Concentration Limits (RMCLs) for many chemical contaminants in water.

The classical method of estimating an ADI involves identifying from dose-response data a "No Observed (Adverse) Effect Level" (NOEL or NOAEL), i.e., a dose level at which no (adverse) affects have been observed in appropriate studies. That dose is then divided by a safety factor such as 10, 100, or 1,000 (depending on the nature and quality of the data available) to produce an ADI.* Risks of adverse effects are assumed to be negligible for daily exposures at or below the ADI, even for susceptible persons. One should note, however, that NOELs and NOAELs can vary with the species tested, number of test animals, and test conditions, including dose levels, duration, and effects looked for. Generally, ADIs have been established for chemicals believed to be systemic toxicants, but not for carcinogens.

TLVs are based on a similar rationale except that they are estimated to be negligible-effect doses for healthy workers exposed 40 hr/week to the substance during the 168 hr week. TLVs have been established both for systemic toxicants and carcinogens by the ACGIH. As a first approximation, a published TLV could be multiplied by 40/168 (0.24) to calculate an approximate (time-weighted average) safe continuous exposure. The derived number is possibly less accurate in establishing an upper risk limit than is the ADI because of the uncertainty of converting from intermittent to continuous exposure. In addition, workers are generally healthier, and therefore probably less susceptible to many adverse effects than is the general population. ADIs are sometimes calculated from a TLV (with appropriate assumptions and conversion of units), but would then have similar uncertainties. RMCLs are based on a rationale similar to those for ADI and TLVs (EPA, 1985b). Dourson and Stara

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* The safety factor is unfortunately sometimes also referred to as an uncertainty factor. Note that an established ADI might be subsequently increased as more reliable data become available that permit a decrease in the safety factor used. Conversely, an ADI might be decreased if data on a new response become available.

(1983) and Dourson (1983) have reviewed the ADI approach, and Moreau and Anderson (1980) and NRC (1980) have discussed its use in risk management. The need for better methods of establishing reliable and defensible ADIs has been discussed recently by Crump (1984b) and Dourson et al. (1985), and alternative methods have been suggested to improve the process.

ADIs and TLVs are of quite limited use in quantitative risk assessments. They state only that an effect is unlikely to occur at or below a stated exposure level. If an ADI or TLV has not been established for a chemical, but results of a good quality chronic study are available that show a clear NOAEL, then the concept might be extended. Considerable care must be taken, however, since the threshold assumption is generally not allowed for carcinogenesis. The ADI says nothing about the degree of response at higher doses. Responses at exposures in the observed range can be estimated directly from the data, but those between the LOAEL or NOAEL and the ADI cannot be easily estimated. The risk may actually still be negligible at exposures much greater than the ADI. The major limitation in the use of either of these procedures is that exposures may be greater than the estimated ADI or TLV so that actual responses (or risks) cannot be directly predicted.

Dourson (1983) has proposed a modified approach to the identification of an ADI that may be useful in extrapolating the dose-response data for chemicals believed to have a threshold. First, using dose-response data (converted if necessary to human equivalents) and an appropriate regression procedure, calculate a dose-response function. Next, calculate the dose estimated to produce a 10% response (d_{10}) and its lower confidence limit. The choice of dose extrapolation model is relatively unimportant, since the common models produce essentially the same curve in the 10 to 90% response region. Then, calculate a modified ADI as the lower confidence limit (of d_{10}) divided by the appropriate safety factor. Next, to estimate effects from a given exposure, use one of three different functions, depending on what the dose is. If the dose is the modified ADI or less, the estimated response is zero. If the dose is d_{10} or greater, the dose is that estimated by the dose-response function. Between these two points (modified ADI of 0 and d_{10} of 0.10), the estimate is the point on the straight line of the log dose-response plot connecting the two points. One limitation on the use of the method in the present application is that if actual exposures are marginally above the modified ADI, the uncertainty in the risk is very high. If the actual exposures are below the threshold, all effects are zero, and comparisons between waste management technologies are reduced to a nonhealth basis such as cost.

(6) Nonparametric methods: If data are too limited to permit parametric methods of assessing health effects, rank-order (nonparametric) methods may still be possible. Some gross variants have been used by the Office of Technology Assessment for classifying waste into hazard categories (OTA, 1983). A review of more refined methods is appended in Calle et al. (undated). One of the options (number 4) considered by OTA (1983), consists of the development and use of an overall hazard classification system as a tool for guiding the regulatory process on hazardous wastes.

An approach used in the Toxic Integration Program (EPA 1981), was applied to exposures specific to 41 chemicals associated with certain industries. The method was also applied to another array of chemicals for the iron and steel industry (Clement Associates, 1982). A different approach, more general in scope and coarser in classification, is being used in the WET risk/cost model, developed by ICF, Inc., for the EPA Office of Solid Waste (EPA, 1983, 1984b).

A related approach is being developed for the National Toxicology Program (NRC, 1982). The system examines available information on the subject chemicals (e.g., production, exposures, chemical properties, and biological effects), analyzes their quantity and quality, and identifies what tests should be done on which chemicals, based on hazard potential and lack of acceptable data. This scheme is expected to be useful in setting priorities for toxicity testing. It may also be adapted as a method for ranking risk, using data that are inadequate for quantification.

The basic drawback of the nonparametric systems is that quantitative conclusions cannot be drawn; only comparisons can be made. If the assessment is to compare courses of action to alleviate a particular problem, then these methods may be useful.

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IX. ESTIMATION AND SUMMATION OF ADVERSE IMPACTS ON EXPOSED POPULATIONS

The objectives of some risk assessments may be met by determining a given health risk to the most exposed individual (e.g., lifetime cancer risk). For many other assessments, however, and particularly for comparison of alternative technologies, an estimation of the total adverse impacts can be essential. After the population(s) likely to be exposed have been identified and the environmental dose(s) have been estimated (as described in Chapter VII), then dose-response relationships developed from the literature base (as described in Chapter VIII) are used to predict the adverse impacts in the exposed population(s). Here "exposed populations" usually refers primarily to humans, but can also include other organisms or nonliving values that could be affected by the environmental contamination. Estimation of human health effects is discussed separately below since they were of primary concern in this study, and more quantitative methods have been developed for them, than for many socioeconomic and ecological impacts.

A. Human Health Impacts

The exposed human population could include members of the general public and individuals exposed occupationally in activities directly related to hazardous waste disposal. Conceptually, the methods of predicting adverse health effects are much the same for both groups or for subgroups within either. The following discussion focuses primarily on public health effects resulting from involuntary, often unidentified, exposures, and notes health effects from occupational exposures only briefly.* In a comprehensive assessment health risks would be integrated over all subgroups. A decision maker would likely be concerned with risks from average exposures for a group and also with risks for the most exposed individuals within a group.

1. Public health effects: The health impact analysis must consider effects in the exposed general population and in any especially sensitive exposed subpopulations.

a. General population: The population at risk can contain exposure subgroups that differ in nature or degree of exposure, e.g., because they live at different locations relative to the pollution source or utilize different water supplies. In addition, the population can also contain subpopulations that are particularly sensitive because of age, sex, general health, genetic deficiency, etc., i.e., they have high toxicological response at a given exposure to the pollutants.

All significant exposure subgroups are first identified and quantified. All significant especially sensitive subgroups also are identified and if possible quantified. If the distributions of the two subgroups are substantially different, and if data are available, it may be desirable to divide the total population into discrete exposure/sensitivity subpopulations before proceeding with the analysis. Probably more frequently, the initial analysis must be made primarily on the basis of the largest exposure groups, and the sensitive subgroups are then considered less quantitatively, as described in the next subsection.

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* Occupational exposures are generally better monitored.

In making the health effects estimation, an average environmental dose for the individuals in each exposure group is identified for each chemical of concern. A risk factor (R) (probability of adverse effect) at this dose (d) is then extracted from the dose-response relationship for the chemical, using either a graphical or mathematical presentation of the relationship as appropriate. This is the average risk factor for individuals exposed at that level. The risk factor is then multiplied by the number of individuals (N) in the exposure groups to calculate the number of cases of the effect for that group.* If there are multiple exposure groups, then a risk factor is identified at the dose level for each group.** The risk factor-subpopulation products are then summed across all exposure groups to estimate the total number of cases for that particular effect:

$$\text{Predicted number of cases} = R_1N_1 + R_2N_2 + \ldots + R_nN_n$$

$$\text{or Predicted total cases} = \sum_{1}^{n} R_i \cdot N_i$$

where: R_i are the risk factors at ith dose (d_i), and

N_i are numbers of people exposed at d_i.

A slightly different version of this calculation has been used by the EPA Carcinogen Assessment Group (CAG) based on a variation of the multistage model for cancer (or other appropriate health effects). The extrapolated probability-dose line is assumed to approach linearity at very low doses (i.e., in the probability (p) range around 10^{-6}), so that the slope is nearly a constant (k).*** Assuming linearity,‡

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* A reviewer commented that the product R_1N_1 is the expected value of risk and is often treated in the literature as a definition of risk rather than using probability as risk or a risk factor.

** A reviewer has noted that simple application of risk factors to a given populations obscures the significant difference in impact on personal/social values between fatalities that are prompt (e.g., vehicular accidents) and those that are delayed (i.e., latent effects).

***CAG actually uses the slope (K) of the "linearized" upper 95% confidence limit rather than the best estimate of risk. The latter is used herein for reasons described in Chapter I.

‡ A reviewer has noted that many researchers believe the assumption of linearity is overly "conservative" in view of growing evidence of greater effectiveness of biological repair mechanisms at very low doses, i.e., the slope may approach zero.

$$p = k\,d \quad \text{or} \quad k = \frac{p}{d}$$

The number of cases of cancer in an exposure group is then calculated by multiplying the individual dose factor, k, by the dose, usually as a concentration (C) and by the number of individuals in the group. The total number of cancer cases can then be estimated somewhat more easily than above, since the summation rearranges to:

$$\text{Predicted total cases} = k \sum_{1}^{n} C_i N_i$$

If the dose-response relationship was in terms of extra cases above background the predicted number will also be for extra cases.

The simplest case for analysis is that of a population uniformly exposed to a fixed level of a single chemical that produces one health effect. For example, a hazardous waste disposal site may contaminate the drinking water supply for a small city with a chemical which can cause nervous system effects upon prolonged exposure. The case becomes more complex as multiple exposure conditions, multiple chemicals, or multiple health effects and multiple subpopulations must be considered.

If the chemical of concern under a given exposure condition produces multiple effects, these must all be considered; calculate each effect with the appropriate risk factors and subpopulations. Note, however, that one or two effects may predominate so that the others can be neglected in the analysis without affecting its validity significantly. The decision criteria cannot be simply stated: decisions will require professional judgment and consideration of available resources and time. If the chemical under different routes of exposure produces the same effect but different response rates, simply sum the estimated effects of each exposure for each subpopulation.

If the chemical under different levels of exposure has multiple effects, then each of these combinations should be considered separately for each subpopulation. If multiple chemicals that cause different effects (as with mixed hazardous wastes) are present, the effect of each on each subpopulation may be required. The effects of similar chemicals may be substantially similar, however, which simplifies the analysis. Similarly, one effect may be of greatest concern because of its nature or because of the level of exposure to the chemical causing it, and the analysis is simplified.

The balancing of disparate effects from alternative technologies is ultimately a part of the risk management process, but the risk assessment can be extended at times to help put this proverbial "apples and oranges" problem in useful context. For example, the number of cases of each type of effect resulting from each option can be tabulated for comparison; the total number of projected fatalities of each can be compared; and the total number of individuals affected nonfatally can be compared. In some cases the decision makers might request that all projected effects be monetized and aggregated for each option for still another basis of comparison.

b. Sensitive subpopulations: If the exposed population contains subgroups that differ greatly in characteristics, then these must also be considered, particularly if they may have a higher response rate (i.e., they may be more susceptible). Generally, the geographical location of fixed structures (e.g., hospitals, schools, nursing homes, recreational areas, and private wells) within the area is sufficient to identify many specific locations where the general population densities can be modified for the subpopulation.

If teratogenic effects are possible from the exposures, then pregnant females are always a subpopulation of concern. In this case a standard birth rate (currently 15.9 live births per 1,000 population in the USA) can be applied to the exposed general population to estimate the number of cases.

A sample worksheet for surveying the potential health effects on a number of subpopulations is given in Figure IX-1. The worksheet addresses health effects from four exposure routes (inhalation, drinking water, dermal, and food) and allows ranking of effects at low, medium, and high, where "low" would be above a de minimis level and "high" might be assigned as a fatal effect by the analyst. Determination of the exposure of the special subpopulations may be considerably more imprecise than that of the generally exposed population; this imprecision would result in a correspondingly greater level of uncertainty in the estimated health effects.

2. Occupational health effects: The method of estimation of actual health effects in exposed workers is conceptually the same as for estimating public health effects, except that the places and conditions of exposure are different and the number of workers to be considered will usually be relatively small. Similarly, subpopulations of exposed workers could be analyzed separately as above if desired in a rigorous treatment.

Assessment of occupational health risks in a quantitative manner can require substantial effort to develop site- and work-station-specific scenarios to estimate the exposures incurred by many different kinds of workers engaged in the various activities involved in treatment, storage, disposal, or transportation of the hazardous wastes and in corrective actions or cleanup operations in case of accidents, spills, fires, or leakage to natural waters. A rigorous comparison of occupational risks across alternative disposal technologies should also include workers involved in construction or maintenance activities unique to any of the alternatives. Specific assumptions might be required regarding the kinds and efficiencies of protective clothing and equipment utilized by the various workers and other worker practices. The effort expended could be high for each hazardous waste.

More qualitative but less costly estimates of occupational risks may be satisfactory for decisions where environmental contamination is the major concern. For example, the treatment, storage, disposal, transportation, and corrective action scenarios for each waste stream can be evaluated to estimate

		PROBABLE HEALTH EFFECTS											
Populations Exposed	Exposure Route	Inhalation			Drinking Water			Dermal			Food		
	Degree	Low	Med.	High	Low	Med.	High	Low	Med.	High	Low	Med.	High
General Public													
Area Residents													
Males													
Females													
Females, Pregnant													
Children													
Fetuses													
Embryos													
Elderly													
Allergic Persons													
Persons Exposed to Other Chemicals													
Workers, Waste													
Workers, Other													
Water Well Users													
Field & Stream Users													
Consumers													
Institutional Residents													
Commuters													
Other Subgroups													

Source: MRI

Figure IX-1 - Sample Exposure-Health Effects Worksheet

the average number of workers exposed. The likely routes and relative levels of exposure can be considered for each, and the relative total occupation risks of alternative disposal technologies then can be estimated. These results are considered along with the relative public health risks and any other factors used in reaching the decision.

B. Ecological and Other Environmental Impacts

Ecological, other environmental and socioeconomic values might incur adverse effects under some technological alternatives, possibly greater than potential health effects. Only brief note can be made here for addressing ecological and socioeconomic effects. A further brief review is given in Appendix C, but a further discussion of environmental and other impacts is beyond the scope of this report.

Conceptually, the approach outlined for quantitatively estimating health impacts on humans could be applied to other species. Practically, however, comprehensive quantification of such impacts will be infeasible in most cases. The variety of domestic animals and crops, wildlife and ecosystems are often simply too great and the data base is usually incomplete. In a few cases, considerable data may be available for quantitative estimation of well-documented effects at given exposures, e.g., crop damage from certain air pollutants; sensitivity of an endangered bird to persistent organics.

Qualitative comparisons of predicted environmental impacts can often be made more easily, and can be a cost-effective aid to the compilation of quantitative information or directly to decision making. Qualitative consideration of the impacts on selected fauna or flora in various ecological niches could be of value in comparing specific hazardous waste disposal alternatives. For example, the potential effects on fish downstream from a hazardous waste disposal landfill could be compared with potential effects on shrimp beds near facilities for transporting wastes to an off-shore incinerator. Particular attention must be given to whether any critical habitats for endangered species are included in the regions where the hazardous waste would be treated, transported, or disposed under any of the technological alternatives.

Socioeconomic effects of alternative choices are monetized for aggregation and comparison far more than are human health and ecological effects. The procedures used have generic acceptance, although analysts may differ on some techniques and assumptions. Substantial differences can occur between parties-at-interest in assigning monetary values to some effects, so that qualitative comparisons may be of help also to the decision makers, who ultimately must balance disparities between effects of different kinds and in reconciling the fact that the costs/risks and the benefits usually have different recipients. Consistency in method and in presentation of results (including uncertainties) for all of the technological options is essential for informed decision makings.

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X. ANALYSIS OF UNCERTAINTIES IN RISK ASSESSMENT OF HAZARDOUS WASTE MANAGEMENT

Deciding between alternative choices of action requires consideration, not only of the anticipated benefits and costs of each alternative, but also of how confident one is in the best estimates of these benefits and costs. In the regulation of technology, a decision maker is particularly concerned that actual health, environmental, or monetary costs may prove to be unexpectedly high (i.e., risks are underestimated) or that the benefits (particularly reductions in risk) may be much lower than anticipated. An analysis of the uncertainties in such estimates is therefore highly desirable. A statement of the degree of confidence the analysts have in estimates of the potential health and environmental effects and the costs of alternative hazardous waste management practices should be an important input into the decision making process.

Concern over uncertainty enters into the decision making process in at least two ways: (a) assuming that the anticipated benefits of an action are achieved, what are the chances that they will be more than offset by unexpected internalized and externalized costs? i.e., what are the risks?; and (b) assuming that one has assessed these risks, how reliable are the methods and data used? That is, how applicable, reproducible, and defensible is the uncertainty analysis of the risk estimates? This chapter presents an overview of uncertainty analysis, discusses sources of uncertainty in analyzing risks from hazardous wastes, and describes the approaches to aggregating and comparing uncertainties. The presentation focuses on the uncertainties in health risks. The resources available for this study did not permit investigation of methods for the analysis of uncertainties in estimates of environmental effects, costs and benefits or of risk-cost-benefit analysis of mitigation actions. Such analyses could be required in many actual decisions. Uncertainties in estimates of cost* are seen more commonly than those of benefits.

A. Overview of Uncertainty Analysis

1. Terminology: The terms "uncertain" and "uncertainty" have substantially different connotations in different popular and professional uses. The root word "certain" indicates a subject is of fixed specific character; an event's occurrence is assured in mind or action; or an issue is indisputably decided. "Uncertain" allows a few additional shades of meaning: a subject is not clearly identified and defined; an event's occurrence is doubtful, indeterminate, or variable in time; or an issue is still to be proved, argued, or decided. "Certainty" indicates a quality or state of being certain, especially on the basis of objective evidence. "Uncertainty" not

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* The initial engineering cost estimates in hazardous waste management are typically stated to be ±30% to ±50%, compared to the uncertainties in health risk estimates typically of at least a few orders of magnitude. Final costs might be an order or magnitude higher than initial estimates in cases of unusual public or regulatory concern.

only indicates a quality or state of being uncertain, but can also imply a statement concerning the quality or quantity of supporting objective evidence.

It is in this last area that usage differs most greatly in the statistical, biological, social, physical, and engineering sciences; in business economics; in policy, legislative, and regulatory actions; and in judicial proceedings. Usage may differ among those describing experimental or historical factual data, those describing most likely future events, and those describing the future as a spectrum of scenarios or probability distributions of possible future outcomes. Some authors describe uncertainty in quite qualitative terms, many describe it in statistical terms, and some use uncertainty synonomously for "risk."* In this study the following definitions are used.

- "Uncertainty" is a statement of the degree to which a system, process, or measurement, or the components thereof are clearly identified or defined, or the likelihood that an event will actually occur.**
- "Uncertainty analysis" is a procedure for attempting to quantify this statement of uncertainty. In particular, we want to quantify the uncertainty associated with estimates of the number of cases of specified adverse human health effects for the alternative waste management scenarios.

2. Approaches to uncertainty analysis: The risk assessment process contains several elements and varies from application to application. Analysis of the overall risk generally requires the analysis of each of several subsets of a sequence of events. The uncertainty is thus compounded by a cascading and propagation of the uncertainties at the subanalysis level. Some of the uncertainties may be of several orders of magnitudes; some uncertainties may seem to dominate the decision; and little hope may exist for reducing key uncertainties by improved data. The problem can thus become far more difficult than textbook examples of decision making under uncertainty where choices are more symmetrical. The analysis of uncertainty may require even greater detail at each element in the risk assessment process than does making point estimates of the risk itself.

Cox and Baybutt (1981) surveyed and compared methods of uncertainty analyses for use in probabilistic risk assessment, and identified five mathematical methods: analytical techniques; Monte Carlo simulations; response surface approaches; differential sensitivity approaches; and evaluation of confidence intervals. Each method has its advantages and disadvantages, according to those authors. Vesely and Rasmuson (1984) state that in nuclear probabilistic risk assessments one needs to differentiate between uncertainties of two major types: (1) physical variability; and (2) lack of knowledge. In contrast, Fiering et al., 1984, distinguished two major types of uncertainty as "analogy" and "cascade." In addition, there is uncertainty over what has, in the past, been true regarding cause-effect relationships vs. what changing relations will occur in the future. Forecasting methods and estimation methodology can differ.

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* The term "uncertainty factor" has also been used synonomously for "safety factor" (see for example Dourson and Stara, 1983).

** A comparison of subjective probability theory vs. statistical frequency theory is beyond the present discussion.

Several approaches to the analysis of uncertainty can be identified. These approaches are used to varying degrees in different fields of analysis, but they are not mutually exclusive and more than one approach can be used in a given analysis. The type of approach that is used and the level at which it is applied will be limited by the completeness in ability to identify all of the causal factors important to outcomes and by the quantity and quality of data. It will also depend on the time and resources available for compiling and evaluating the information. A partial list of approaches is shown in Table X-1 in generally increasing order of data and time requirements; the list is intended to be illustrative, not necessarily complete (Lawless, 1984). These approaches are discussed briefly below, followed by several considerations that may affect the choice of approach in a specific application.

TABLE X-1

SOME APPROACHES TO UNCERTAINTY ANALYSIS

Approach	Information Requirements
Qualitative discussion	Useful when causal understanding, data, time to compile information, perform detailed analyses, or seek expert judgment is limited.
Expert judgment analysis	Requires appropriate cross section of technical experts; requires techniques for eliciting and combining their opinions based on subjective evaluation of both direct and indirect data on cause-effect relationships.
Sensitivity (parametric) analysis	Mathematical (or experimental) model of relationships; reasonable estimates of likely variance in key data/information sources.
Statistical analysis (many kinds)	Extensive experimental or historical data or results; formal statistical methods.
Propagation or cascading of errors analysis	Mathematical formulation of problem analysis; measure or estimate of uncertainty of each data component.

a. Qualitative discussion: A qualitative approach can be helpful in evaluating uncertainty, particularly if data of adequate quality are limited or if time is unavailable to compile information, perform rigorous analyses, or seek expert judgment. Qualitative judgments may also be based on considerable amount of data that are indicative of cause-effect relationships not quantitatively and scientifically demonstrable in a rigorous sense.

A systematic identification and discussion of possible causes of errors and uncertainties help to establish the general framework (Lawless, 1982). A tabular outline and qualitative discussion of component uncertainties may be of considerable value. Rough estimates of the relative uncertainties of various factors may permit a rank ordering of factors, identification of key factors, or a first approximation of the relative risk of alternative decisions. Fiering and Wilson (1983) have examined the potential for estimating risks by analogy. Lawless et al. (1984a, 1986) have investigated semi-quantitative approaches to comparing risks and their uncertainties.

b. Expert judgment analysis: If data are substantially deficient or the analysis is not amenable to formal mathematical methods, uncertainty may be evaluated by soliciting expert opinion regarding either an absolute value or the uncertainty of stated values. This solicitation can utilize informal contacts, a formal survey instrument, or an approach with feedback, such as the Delphi. Several steps that could be used in the expert judgment approach to uncertainty analysis in risk assessment are summarized below:

* Assemble panels of experts in key areas of problem analysis. These panels should have expertise in several applicable areas, such as: pollutant sources; environmental transport and fate; exposure-to-dose conversions; dose-response analysis; microbiology; genetics; enzyme chemistry; and epidemiology. At least five panelists per area may be needed to get a representative sampling on some issues.

* Obtain experts' best estimates and opinions of uncertainty on issues of concern, such as: available data; absolute and/or assumed values; methods of analysis; calculated or derived results.

* Plot distributions of opinions for each area/panel

* Feedback results to panelists; request second opinion

* Summarize uncertainty analysis

Selection of a suitable cross-section of unbiased, credible panelists may be difficult for some topic areas. There are no "instant experts" and many potential panelists may have already taken opposing, strongly polarized or even controversial positions on a subject. Alternatively, the experts may have similar backgrounds that yield narrow perspectives of the uncertainty or they may have low credibility because of previous events. The analyst must be aware of such possibilities and, if necessary, note them appropriately in the assessment report. A sensitivity analysis over a wider range of conclusions may be helpful.

Monte Carlo simulation approaches to using expert-estimated costs in environmental areas has been described (Goddard, 1981, 1983; Klee (1983). Publications were not found that illustrated the application of the technique to environmental health risks, where the uncertainty of variables may be orders of magnitude greater than in cost or engineering reliability applications. The general value and limitations of using expert judgment in risk assessment have been discussed by Hammond et al. (1984) and Morgan et al. (1984).

c. Sensitivity (parametric) analysis: This method is especially useful in gaining a better understanding of how important the range of uncertainty is to the decision regarding different causal scenarios contributing to the uncertainty. Sensitivity analysis can be structured as either an experimental or hypothetical system of causal relations, often using mathematical models. The relative responsiveness of an observed or derived result to changes in various inputs or assumptions is determined by systematically varying these inputs or assumptions in turn and repeating the calculation or analysis. The variation of inputs preferably is statistically designed, and the analysis of results preferably includes statistical techniques such as analysis of variance.

An experimental design should be used to specify how the various input parameters are to be varied. The design should usually be of a factorial nature, varying several parameters simultaneously. If the number of input parameters is large, an incomplete design, such as a Latin square might be employed. Analysis of variance, matched to the design chosen, would be used to assess the sensitivity of the model to each input parameter (factor main effect) or combination (interaction). In general, the computations would be performed on a computer, with calculation of the model performed at each design point and stored for use in the analysis of variance program. Using even a micro- (or personal) computer would enable the calculations to be performed in a relatively short time unless the model is extremely complex. The major effort would be in setting up the design and in programming.

In nonexperimental studies scenario construction is sometimes used to establish a self-consistent set of related parametric values for analysis. Modeling and simulation analyses (e.g., Monte Carlo) may sometimes be regarded as forms of parametric analysis for addressing uncertainty, but these are really substantial and overlapping classes of techniques used primarily for predictive purposes (they may also be used for descriptive purposes).

In some situations the experimental design approach is not feasible. This may result because the number of combinations of factors is so large that even incomplete designs would be impractical. Alternatively, it may be that many of the combinations called for in an experimental design are not realistic or could not occur in practice because of dependencies among the input parameters. In these situations an alternative approach may be the use of Monte Carlo simulation. The relationships of the parameters are specified, together with distributions of these. Random number generators are used to select the combinations of parameters to be used in the calculations. Again, a computer is utilized. Programming effort will be more extensive, and description of the appropriate input parameter relationships and distributions will require extensive work.

Vesely and Rasmuson (1984) state that uncertainty analysis goes beyond sensitivity analysis in that probabilities or confidences are assigned to different sizes of changes that can occur.

d. Statistical analysis: Statistical analysis is a broad collection of techniques rather than a single approach. If extensive experimental or historical data are available, various rigorous statistical analyses can be used to quantify study parameters and to estimate uncertainties in these quantifications. Statistical analysis is particularly useful in evaluating random errors among values in sets of data. Formal statistical methods and tests can be applied to determine deviations, probability distributions, confidence limits, goodness of fit to theory, etc. Statistical techniques are often combined with specific models and simulation methods to analyze uncertainty. Similarly, application of Bayesian statistics may be helpful in combining expert judgment with limited observational data to estimate uncertainty. An extensive literature is available.

One may identify three main types of error that occur in statistical analysis. The one most commonly dealt with is random variation. Often this is the result of taking a random or probability sample of a population. A second source of error might be termed systematic data bias. This arises if the data are not a random or known probability sample, but rather a selected or nonrepresentative subset. This may be caused by incomplete or inappropriate sampling frame and by nonresponse or inappropriate data gathering techniques. A third type of error is model bias. This arises because all mathematical or statistical models are simplifications and approximations. Different models will give different results and, in the absence of knowledge about which model is the better representation of the situation, this will add to uncertainty.

Statistical analysis can give good estimates of the sampling variability in the data. The results generally depend strongly on the models assumed. Comparison of results assuming different statistical models in a sensitivity analysis can indicate the robustness of the results to the model assumptions. However, the possible errors that arise from using an incorrect or incomplete model are difficult to address by statistical estimation. Further, if there are biases in the data, these may also be difficult to estimate quantitatively.

e. Propagation or cascading of errors: If a result is being derived from a series of measurements or sources of data, the uncertainty in each measurement or data point is first estimated. The overall uncertainty in the derived result can then be calculated by appropriate arithmetic or geometric combinations. The process is variously called the propagation of errors or cascading of errors method.* Considerable literature is available on error analysis.

Two cases may exist: the variables may be either independent or dependent. Analyses with substantial interdependence among variables are more difficult. Dependence may operate to either increase or reduce the error in the final result. The variance (var) of the sum of two variables, x and y, is given by the equation

$$\text{var}\,(x + y) = \text{var}(x) + \text{var}(y) + 2\ \text{covar}(x,y)$$

where the covariance of x and y (covar(x,y)) may be positive or negative. If x and y are independent, the covariance is zero. The covariance may be zero without x and y being necessarily independent.

If one sums 3 variables, the variance of the sum becomes

$$\text{var}(x+y+z) = \text{var}(x) + \text{var}(y) + \text{var}(z) + 2\ \text{cov}(xy) + 2\ \text{cov}(xz) + 2\ \text{cov}(yz)$$

Complexity increases rapidly as the number of variables increases. In general, the sum has n^2 terms**

$$\text{var}\Big(\sum_{i=1}^{n} x_i\Big) = \sum_{i=1} \sum_{j=1} \text{cov}(x_i,x_j), \text{ where } \text{cov}(x_i,x_i) = \text{var}(x_i)$$

3. Considerations affecting choice of approach: The choice of approach to uncertainty analysis in a given application will depend on one or more of several characteristics of the problem at hand. Some commonly considered characteristics are indicated in Table X-2.

B. Sources of Uncertainty

The analysis of uncertainty of the risk estimates of alternative regulatory decisions involving hazardous materials must consider both systematic errors and random errors. The former may be more important than the latter in risk assessment since systematic errors introduce unidirectional biases that do not tend to cancel each other as in the case of bidirectional random errors. Systematic sources of uncertainties include:

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* Second order subjective probability estimates, based on uncertainty surrounding the first order estimate of a probability density function, are omitted here.

** A reviewer commented that because the cascading of errors leads to an increasingly wider range of uncertainty, use of a Monte Carlo simulation that integrates the cascading probability density functions will provide an aggregate p.d.f. that exposes the thinness of long tails created by the integration. Thin tails usually represent de minimis risk that can be ignored.

TABLE X-2

CONSIDERATIONS AFFECTING CHOICE OF APPROACH TO UNCERTAINTY ANALYSIS

- Information and Data Needed for Productive Application, e.g., quality, quantity, difficulty of collection, level of detail required
- Most Applicable Range of Risk, e.g., low probability events of greater significance than de minimis risk
- Most Applicable Range of Uncertainty
- Levels of Disaggregation and Aggregation Desired or Permitted
- Ability to Handle Complex Interactions of Risk Components
- Predictive Value with Increasing Time Horizons
- Modes Available for Expressing Results to Experts and Laypersons
- Credibility/Defensibility
- Applicability to Risk Management Concerns
- Ability to Address Effects of Corrective Actions and Reversibility
- Ability to Appraise Value of Additional Information
- Ability to Identify Research Needs
- Difficulty of Bounding the Analysis
- Ability to Complement Other Methods
- Likelihood Utility of Approach Will Be Improved

- Assumptions made in structuring the problem so it can be analyzed
- Limitations in the accessibility, quality, and quantity of the available data, and in the comparability of data for the alternatives being assessed
- Applicability of available methods and models for performing the risk assessment
- Applicability of methods for accounting for temporal disparities, quantification and discounting of nonmonetized values, and value system differences
- Reliability of interpolation and extrapolation techniques used
- Allowance for corrective actions

The sources of uncertainty in assessing the risks of hazardous waste storage, treatment, and disposal are numerous. Uncertainty arises from most of the activities of the assessment. These sources may be categorized into seven broad functional areas (factors) that reflect major activities in a comprehensive comparative risk assessment. Each factor is composed of several subfactors or variables. Some of these are discussed below. A checklist was provided in Chapter IV.

1. Scenario definition and applicability: Results of the risk assessment will inevitably be affected by the way the particular scenario is structured for analysis. Most problems in decision making can be reduced to a format of alternative scenarios. The uncertainty associated with applying the results will be a reflection of the detail built into the scenario, which may range from quite simple to quite detailed. The fewer and more similar the number of scenarios, probably the smaller the relative uncertainty across scenarios. Likewise, the smaller the range of effects considered, the smaller and more homogeneous the population (or environmental values) at risk, and the more clearly defined the science and technology, *ceteris paribus*, the less the uncertainty. Finally, the more nearly a scenario addresses real world policy questions, the more value the uncertainty analysis should have in making decisions. While the various conditions that are defined in developing a scenario are often subsequently taken as fixed values and excluded from the analysis, one should not forget them in the final assessment because they may have greatly shaped the outcome.

2. Pollutant release: This term refers to the source strength of the pollutant; that is, it includes information on the probability and magnitude of release of given pollutants to the environment over time. The term covers several factors that are sources of uncertainty. These include: general characteristics and quantities of waste being treated and disposed; knowledge of the chemical constituents of the waste; knowledge of the properties of the constituents, particularly those affecting release to the environment; geographical, geological, and meteorological settings of the treatment and disposal site; performance of the treatment disposal technology;

and identity, quantity, and rate of hazardous material released to environmental media off-site. These release factors may include several subfactors, such as: time to failure of a liner, volume of leachate, and quantity of constituent leached for a landfill; destruction and removal efficiency for a particular chemical in an incinerator; and frequency and magnitude of accidental spills in transporting hazardous wastes. Analysis of only the air emissions from a treatment, storage, and disposal facility still requires consideration of many uncertainties (Wallace et al., 1987).

3. Environmental transport and fate: The quantity and rate of hazardous constituents moving through the air, water, or soil from the point of release to human receptors depend on several factors that may be sources of uncertainty. These include: applicability and completeness of environmental monitoring data; applicability of models that simulate movement through the media; decomposition, degradation, or stabilization processes that render the constituent harmless or immobile; and tendency of the constituent to bioaccumulate in the flora and fauna or to biomagnify in food chains. The more complete the data base and the more verified the models, the smaller the uncertainty.

4. Exposure prediction: This involves estimation of the range in space and time that the pollutant interacts with environmental receptors (as determined by analysis of pollutant release and environmental transport) and the number of receptors at those points (as determined by data on population distribution and lifestyles). A source of uncertainty in many exposure assessments is the range of exposures that may exist for even a narrowly defined population. Exposures are not necessarily the same as a known toxicological dose. Hence, assumptions must be made to convert the predicted exposure to a dose. These assumptions require consideration of routes, chemical and physical forms, maximum or average concentrations, and frequencies and durations of exposures. All of these are subject to uncertainty.

5. Health effects data and model availability: An important uncertainty factor is the quantity and quality of the data describing the health or environmental effects of the constituents of concern under known, controlled conditions of exposure. A related factor is the availability and suitability of models for making the necessary extrapolations or the development of a model that will be applicable. This factor contains many widely discussed uncertainties associated with extrapolations across dosage regimen, species, and other factors. Predictions of health effects can require consideration of absorption, metabolism, excretion and other toxicokinetic processes. Ideally, the literature will contain dose-response data for exposures approximating or extrapolatable to those occurring environmentally, but less desirable alternative approaches for utilizing incomplete data sets may be required. Problems of uncertainty in data sets and in applicability of available models were discussed at some length in Chapter VIII. The more complete the data base, generally, the smaller the uncertainty. The more verified or defensible the models, the smaller the uncertainty.

6. Health impact estimation and summation: Estimation of a given health effect for an exposed individual requires a multiplication of a given predicted environmental exposure level times a dose-response factor for that

level. The effect must then be integrated over all persons exposed at that level and at all other levels. Hence, uncertainties exist over the numbers of persons in each exposure group and the levels of their exposures. In addition, all especially sensitive subpopulations must be identified and assessed. Further, if the chemical of concern has multiple effects at different levels, these must be integrated across the entire exposed population, again with consideration as necessary of sensitive subpopulations. In general, the more homogeneous the population and exposures, and the fewer the kinds of health effects, the less the uncertainty.

C. Aggregation of Uncertainties

The estimated risk to human health of each waste management disposal scenario will depend on the analysis of risk-related terms or factors for each of a number of events. The uncertainty in the overall risk estimate of each can be derived, in theory, from an appropriate combination of the uncertainties of the identified variables according to the principles of error analysis. The appropriate manner of combining the uncertainties depends on the relationships among the variables.

Arithmetical aggregation: If the occurrence of any of a number of events results in risk or existence of any factor or variable poses a risk, then their risk terms are additive; i.e., the total risk (R_T) is a simple sum* of the risks (R_i) of the separate events or variables. That is,

$$R_T = R_1 + R_1 + R_2 + \ldots R_n$$

The uncertainty can be stated in two ways. If the sources of possible errors are independent and one lets σ_i be the standard deviations associated with R_i, then the total standard error is given by an equation for summing the standard deviations as follows:

$$\sigma_T = \sqrt{\sigma_1^2 + \sigma_2^2 + \ldots \sigma_n^2}$$

This relationship does not depend on the form of the probability distributions for the events or variables, so long as they have finite variances. If the composite error is approximately normally distributed, then multiplying σ by a factor allows one to express the uncertainty as a confidence interval, i.e., ±σ has 68% confidence limits, ±2σ has 95% confidence limits, ±3σ has 99% confidence limits, etc.

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* If the events are not mutually exclusive, then the simple sum must be adjusted for this fact, i.e., R (A or B) = R (A) + R (B) - R (A and B), where R = probability of effect in a given time interval.

The standard error is not the only way of expressing an expected or average error. A key concept is the distinction between an expected or average error in a set of statistical data and an actual error in predicting a future event. For example, if a risk analyst estimates that a given accident would lead to a spill of hazardous waste of size x, but subsequently an actual accident gave a spill of size s then the actual absolute error e of the estimate was

$$e = x - s$$

At the time of making the estimate, however, both s and e were unknown. The analyst might calculate many reasonable values of s to estimate an average error, i.e., express the average error as a function of s

$$\text{Ave } |e| = \int |x-s| \, dF(s)$$

The standard deviation is an averaging process.

Another consideration in aggregating uncertainties involves the "worst case" scenario, which arises from concern that events or variables will combine in a way that produces a near maximum rather than average error, i.e., the possible errors are strongly biased in one direction. The total error is then the sum of the absolute values of the component errors. Although such combinations are highly unlikely, they are possible. The regulatory decision maker is frequently faced with the difficult choice of whether or not to consider such combinations and, if so, how. In practice, the issue is resolved on a case-by-case basis. This topic is discussed further in the next section.

Geometrical aggregation: If all of several events in a series must occur simultaneously or in sequence for total adverse effects to occur, then the risk factors are multiplicative according to the principles used in propagation or cascading of errors analysis (as discussed in Section A.2.d); i.e., the overall risk is a product of the separate risk factors.

In assessing the risk of hazardous waste management technologies, the overall risk (R) can be mathematically structured as a product of a series of risk-related factors (F), each representing one of the several major factors discussed in Section B. The magnitude of the risk* can then be calculated from the estimated values of the factors, assuming that each is positive and all are probabilistically independent.** The relationship may be stated as a simple product or as a logarithmic sum:

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* This is an absolute rather than relative risk between alternatives.

** If the factors are not independent, then the multiplication of probabilities is conditional, i.e., in general, $P(F_1 \cap F_2) = P(F_1)P(F_2/F_1)$; if F_1 and F_2 are independent, then $P(F_1 \cap F_2) = P(F_1)P(F_2)$. In the absence of independence, the factors are viewed as conditional probabilities.

$$R = F_1 \times F_2 \times \ldots F_n$$

$$\text{or } \log R = \log F_1 + \log F_2 + \ldots \log F_n$$

The several factors may in turn depend on one or more other subfactors that reflect the variables (v). If all the variables within a factor are essential, the factor is a product of the absolute values of the variables, each variable being positive and independent. In general, however, all of the variables will not be essential. For example, a factor, F_i could be of the form $av_1v_2 + bv_3^2$. The contribution of all the variables to the risk must then be calculated by a combination of additive and multiplicative operations. The analysis therefore becomes problem-specific at this point.

If the uncertainty in each F_i term above is expressed as a variance,* then the uncertainty in log R can be expressed as the sum of the uncertainties of the component factors. If the F_i factors are independent, then the equation is:

$$\text{var}(\log R) = \text{var}(\log F_1) + \text{var}(\log F_2) + \ldots \text{var}(\log F_n)$$

or

$$\text{var}(\log R) = U_1^2 + U_2^2 + \ldots U_n^2$$

where $U_i^2 = \text{var}(\log F_i)$

If the F_i are not independent, then

$$\begin{aligned} \text{var}(\log R) &= \sum_i \sum_j \text{cov}(\log F_i, \log F_j) \\ &= \sum_i \text{var}(\log F_i) + 2\sum_{i<j}\sum \text{cov}(\log F_i, \log F_j) \end{aligned}$$

Little can be said in general about the effect of the covariance terms; they may be positive or negative.

Since log R is a sum of n terms, each of which is based on an estimated value, the error in the estimate of log R will generally be approximately normally distributed. This follows from a version of the central limit theorem (e.g., if the estimates of log R are independent with finite variances and the number of terms is large). The uncertainty may be expressed if desired as a range or confidence interval by the expression

$$\log R \pm t\sqrt{\text{var}(\log R)}$$

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* Variance, the square of the standard deviation, may be used if bias is absent; a mean square error is used if bias is present.

where t is a value from a probability distribution table corresponding to the degree of confidence desired.* If log R is approximately normal, the t distribution is appropriate.

Alternatively, the expression can be written

$$\log R \pm tU$$

where U is a total uncertainty factor, $U = \sqrt{\mathrm{var}\ (\log R)}$

Substituting in the log R equation above and converting back to the risk scale by taking antilogs yields a relationship showing the estimated risk and its upper (R_u) and lower (R_ℓ) limits (i.e., its uncertainty range):

$$\text{Risk range, } R_u, R_\ell = \left| \begin{array}{l} R \bullet \mathrm{antilog}\ |t|\ \sqrt{\mathrm{var}\ (\log R)} = R \bullet \mathrm{antilog}\ |t|\ U \\ R \div \mathrm{antilog}\ |t|\ \sqrt{\mathrm{var}\ (\log R)} = R / \mathrm{antilog}\ |t|\ U \end{array} \right.$$

where $|t|$ is the absolute value of t. Converting to base 10 logarithms yields

$$\text{Risk range} = \left| \begin{array}{l} R \bullet 10^{|t|U} \\ R \div 10^{|t|U} \end{array} \right. \qquad \text{or Risk Range} = R \bullet 10^{\pm|t|U}$$

But from above, $U^2 = U_1^2 + U_2^2 + \ldots U_n^2$

so that

$$\text{Risk range} = R \bullet 10^{\pm|t|\ (U_1^2 + U_2^2 + \ldots U_n)^{1/2}} \qquad (+ \text{ for } t > 0;\ - \text{ for } t < 0)$$

Note that parameter t is actually a decision parameter, reflecting the degree of confidence that a decision maker would want in the data and information available.** For some decisions, a value of t of ±1 may be adequate, whereas for others, additional analyses, sampling, or other research may be required to meet a desire to set t = ±3 (99.3% confidence limits). The value specified for t therefore reflects risk aversion or acceptance levels.

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* t is related to the confidence interval. If the estimates of log R have a normal distribution, then t = ±1.96 would give the 95% confidence level and t = ±1 would give a confidence interval of 68.3% (i.e., one standard deviation).

** If the confidence coefficient is held constant, $|t|$ varies with the distribution (i.e., normal or various nonnormal distributions). Alternatively, if $|t|$ is fixed, the coefficient varies by distribution.

Decisions involving the comparisons of alternatives are relatively insensitive to the value of $|t|$ assigned. That is, if one is comparing the risks of four alternative hazardous waste disposal technologies for a given waste, one would want to use the same value of t in the analysis of each, but the comparison can then be made about as well with all uncertainty ranges reflecting 68% confidence limits ($t = \pm 1$) as with all reflecting 95% limits ($t = \pm 2$), or 99% limits ($t = \pm 3$). In fact, the use of higher confidence intervals may merely increase the overlap of risk ranges for the alternatives, as depicted in Figure X-1, with uncertain effect on decision making.* As a convenient first approximation therefore $|t|$ can be usefully assumed to be unity ($t = 1, -1$). The relationship above becomes:

$$\text{Risk range} = R \cdot 10^{\pm (U_1^2 + U_2^2 + \ldots U_n^2)^{1/2}}$$

The composite worst case scenario is a further consideration in multiplicative aggregation of uncertainties as it is (see above) in arithmetic aggregation. In geometrical aggregation, however, the need to consider such worst case combinations in regulatory decision making may be substantially reduced. For example, if five events must occur in sequence or together for an adverse effect to occur, one need not control the risk factor for each at a probability of one in a million (10^{-6}) or even 0.1% (10^{-3}) in order to assure reasonable public safety. Such stringent controls would reduce the overall risks to extremely low levels (one in 10^{30} and one in 10^{15}, respectively**), but would probably be quite costly. If one wanted to control the overall probability at, say, 10^{-7}, then each individual risk factor would need to be controlled at an average probability of $10^{-1.4}$ or about one in 25. If one then wanted to allow an extra margin of safety--say corresponding to an extra order of magnitude on the overall probability (i.e., 10^{-8}), one would control the individual risk factors at about one in 40.

D. Relative Uncertainty and Risk

In actual application, the absolute magnitudes of the uncertainty of some variables may be unknown. In addition, the aggregated risks across a scenario may be very high. In some cases these may not be intractable problems. For example, if one is comparing scenarios both of which contain the highly uncertain variable in the same way, or contain many (but not all) of the same variables, then a calculation of the relative magnitude of the uncertainties and the risks may be helpful (e.g., in ranking of risks of alternative waste management methods. In some cases also, the sensitivity analysis may show that one risk factor dominates the range of estimated risk, so that uncertainties in some other factors will not significantly influence

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* A reviewer noted that because of the high uncertainties with hazardous waste disposal and this increasing overlap between alternatives, a sensitivity analysis of the more extreme (but still credible) adverse assumptions may be more useful than an exhaustive effort to quantify all uncertainties.

** Calculated from $(1/10^6)^5$ = one in 10^{30}, or 10^{-30}.

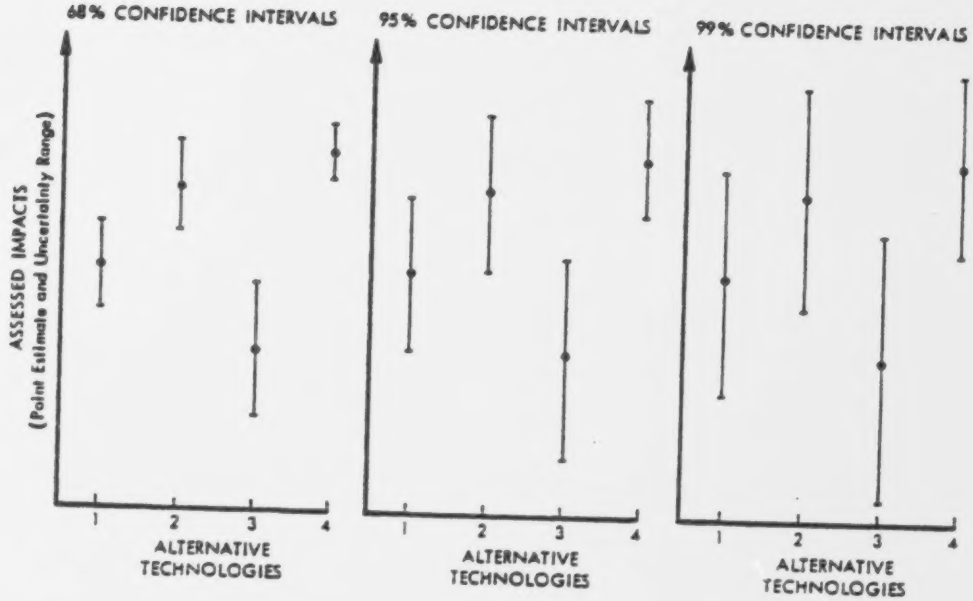

Figure X-1 - Comparison of Uncertainties at Increasing Confidence Intervals for Assessed Impacts of Hypothetical Alternative Technologies
Source: Lawless, 1986

the decision. Table X-3 is an example of aggregation of total, comparative, and relative uncertainties in site-specific health risk assessment of four disposal alternatives for mercury-contaminated brine muds from chlor-alkali manufacture (Lawless et al., 1984b).

E. Use of Surrogates in Comparative Risk Assessment

A prediction of the number of cases of cancer or other adverse health or environmental effects that would result on a global, national or site-specific local basis from activities involving a chemical is generally difficult to make quantitatively and accompanied by substantial uncertainties. Governmental agencies have therefore frequently used surrogate indicators for regulatory purposes that are often less difficult to develop and more easily defended. The surrogates used vary with the chemical technology involved and the regulatory setting, but examples include:

- Risk to the average or most exposed resident, worker, or consumer on a partial (or whole lifetime) basis as a surrogate for total effect.
- Intrinsic toxicity characteristics as a surrogate for risk. Chemical class is occasionally a surrogate for toxicity.
- Exposure as a surrogate for risk.
- Population potentially exposed as a surrogate for actual exposure.
- Environmental transport and fate characteristics as a surrogate for exposure, including mobility, environmental persistence in air, water and earth, and bioaccumulation factors.
- Release or escape to the environment as a surrogate for exposure through environmental routes.
- Production, distribution and use patterns as surrogates for release to the environment.

Most of these surrogates have found use at times for regulation of certain aspects of specific chemicals, but their value may be most useful in comparative assessments, such as those considered in the present study of hazardous waste management. For example in some cases, alternative waste management option may pose risks to the same populations by the same chemical. Comparison of the relative emission rates might yield sufficient information to rule out one option. In other cases the relative sizes of the populations likely to be at risk might be critical. In still other cases the relative toxicities of chemicals that might be released may differ sufficiently to be the basis of a choice. Note that decisions based on surrogate indicators can be reconsidered latter on a case-by-case basis if preferred, or if time and resources have permitted comprehensive comparative risk assessments of the alternative technologies, regulations or standards.

TABLE X-3

AGGREGATION AND COMPARISON OF UNCERTAINTIES IN SCENARIOS FOR DISPOSAL OF MERCURY-CONTAINING BRINE MUDS

a. TOTAL UNCERTAINTIES

Scenario	Release factor	Transport factor	Exposure factor	Dose-response factor[a]	Health effects estimation factor	Total uncertainty
Dewater and landfill	$10^{1.4}$	$10^{1.8}$	$10^{0.7}$	$10^{2.1}$	$10^{0.3}$	$10^{3.2}$
Hypochlorite extraction						
Reprecipitated HgS	$10^{0.5}$	$10^{1.6}$	$10^{0.7}$	$10^{2.1}$	$10^{0.3}$	$10^{2.8}$
Extracted mud	$10^{0.7}$	$10^{1.8}$	$10^{0.7}$	$10^{2.1}$	$10^{0.3}$	$10^{2.7}$
Stabilization and landfill	$10^{2.0}$	$10^{1.8}$	$10^{0.7}$	$10^{2.1}$	$10^{0.3}$	$10^{3.5}$
Surface impoundment	$10^{1.6}$	$10^{1.8}$	$10^{0.7}$	$10^{2.1}$	$10^{0.3}$	$10^{3.3}$

b. COMPARATIVE UNCERTAINTIES

Scenario	Release factor	Transport factor	Exposure factor	Dose-response factor[a]	Health effects estimation factor	Total comparative uncertainty
Dewater and landfill	$10^{1.4}$	$10^{1.8}$	NA	NA	NA	$10^{2.3}$
Hypochlorite extraction						
Reprecipitated HgS	$10^{0.5}$	$10^{1.6}$	NA	NA	NA	$10^{1.7}$
Extracted mud	$10^{0.7}$	$10^{1.8}$	NA	NA	NA	$10^{1.9}$
Stabilization and landfill	$10^{2.0}$	$10^{1.8}$	NA	NA	NA	$10^{2.7}$
Surface impoundment	$10^{1.6}$	$10^{1.8}$	NA	NA	NA	$10^{2.4}$

c. RELATIVE UNCERTAINTIES[b]

Scenario	Release factor	Transport factor	Exposure factor	Dose-response factor[a]	Health effects estimation factor	Total relative uncertainty
Dewater and landfill	10^{0}	10^{0}	NA	NA	NA	10^{0}
Hypochlorite extraction						
Reprecipitated HgS	$10^{-0.9}$	$10^{-0.2}$	NA	NA	NA	$10^{-0.6}$
Extracted mud	$10^{-0.7}$	10^{0}	NA	NA	NA	$10^{-0.4}$
Stabilization and landfill	$10^{0.6}$	10^{0}	NA	NA	NA	$10^{0.4}$
Surface impoundment	$10^{0.2}$	10^{0}	NA	NA	NA	$10^{0.1}$

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[a] Neurotoxic effects.

[b] $$\text{Relative uncertainty} = \frac{\text{Uncertainty factor for Scenario X}}{\text{Uncertainty factor for Dewater and Landfill Scenario}}$$

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APPENDIX A

RISK ASSESSMENT TERMINOLOGY

The voluminous literature relating to risk-related decision making and risk management under uncertainty is characterized by wide variation in terminology and, at times, serious semantic inconsistencies. This situation reflects the imprecision of current usage of risk terms and the variance between disciplines, scientific committees, agencies, and even between different parts of a single government agency, including the Environmental Protection Agency (EPA). This appendix provides: (a) an historical perspective on risk assessment terminology; (b) excerpts on risk assessment requirements under RCRA; (c) useful definitions of terms appearing in this report.*

1. Historical Perspective

Interest in considering and coping with risks originated many centuries ago in maritime and life insurance applications and in games of chance; it expanded rapidly after the development of probability theory about 200 years ago (Covello and Mumpower, 1985). Applications were subsequently made in public health, business economics, engineering, and other fields where statistical data were gathered. Particularly pertinent to the present study were studies concerned with the human health impacts of ionizing radiation (x-rays, ultraviolet radiation, radio-isotopes, etc.). Probabilistic analysis methods have been studied extensively in support of nuclear power, defense, and aerospace development during the past three decades--a period in which efforts to assess the health effects of chemicals have become increasingly intense. In the United States, several government agencies have spurred the development and application of methodologies for assessing the risks of chemicals: first, the Food and Drug Administration and then others such as the Environmental Protection Agency, the National Institutes of Health, the Nuclear Regulatory Commission, and the National Science Foundation.

The need to estimate technology-related risks and to regulate them appropriately have been the subjects of countless studies. Committees of the National Research Council (National Academy of Sciences) alone have published numerous studies on the regulation of chemicals in the last decade. Some have focused on principles for evaluating or making decisions on environmental chemicals (NAS/NRC, 1975; NRC, 1975). Others have focused on pesticides (NRC, 1977b; NRC, 1980a), drinking water (NRC, 1977c, 1980b), food additives (NRC, 1979), or related cancer-causing agents (NRC, 1980c). Three committees focused on the process and practice of decision making in the EPA (NRC, 1977a) and in government agencies in general (NRC, 1982; NRC, 1983). The Office of Technology Assessment also has reviewed methods for assessing environmental health risks (OTA, 1979, 1981, 1984). The Office of Science and Technology Policy published a lengthy review of the science and principles associated with assessing chemical carcinogens (OSTP, 1985). In addition, dozens of books have been published based on symposia and conferences about risk (see references and related publications at end of this appendix).

** EPA recently updated and expanded its "Glossary of Environmental Terms" (EPA, 1988) after most of the work of this study was completed.

The terms "risk analysis" and "risk assessment" are sometimes used interchangeably and sometimes not. According to dictionary definitions, "analysis" (from 'to dissolve') implies separation of a whole into its component parts, followed by identification and quantification of the parts. "Assessment" (meaning 'to assist the office of judge') implies appraisal, valuation, judgment, and a summing up. The journal of the Society for Risk Analysis uses the terms interchangeably.

'Risk analysis' evolved from the Atomic Energy Commission's studies of potential failure modes in nuclear power plants and their consequences (USAEC, 1957 and USNRC, 1974) and the Department of Defense's efforts in the 1950's and 1960's to reduce cost overruns on major systems such as the C-5A and F-111 planes (CRS, 1972). The AEC used the term 'probabilistic risk analysis' (PRA) in connection with highly numerical efforts to quantify risks. More recently, however, PRA is often defined as assessment.

Otway and Pahner (1976) defined risk assessment as having two components, risk estimation and risk evaluation. Kates (1978) considered it to have three elements, identification, estimation, and evaluation, while Rowe (1977) defined its two components as risk determination (including identification and estimation) and risk evaluation (including aversion and acceptance). Porter et al. (1980) equated risk assessment with risk-benefit analysis and utilized Otway and Pahner's structural description. Conrad (1980b), Greer-Wootten (1980), and also a group of International Atomic Energy Agency researchers (Cullingford et al., 1982) defined the risk assessment process as having three main elements: risk analysis (i.e., estimation); risk evaluation; and risk management. The U.S. Nuclear Regulatory Commission now describes its probabilistic risk assessment procedure as composed of systems analysis and containment analysis, each of which had several component steps (USNRC, 1984).

In contrast, Moss and Lubin (1981) and a recent National Research Council committee chaired by Raiffa (NRC, 1982) considered risk analysis to be composed of two aspects: risk assessment and risk evaluation. Pearce (1981) considered risk analysis to be a special case of cost-benefit analysis. Moghissi (1984) defined risk analysis to include both risk assessment and risk management.

Environmental risks of chemicals were specifically reviewed by Conway and coauthors (Conway, 1982). Conway defined risk assessment to include the evaluation of the scientific data collected and examined during an analysis step and evaluation of the social, economic, and political factors (including beneficial effects) considered in reaching decisions on prohibition, control, or management of chemicals in the environment.

A study group of the Royal Society (1983) also divided risk assessment into risk estimation and risk evaluation. Estimation was subdivided into three steps: identification of outcomes; estimation of magnitude of the associated consequences; and estimation of the probabilities of these outcomes. Risk evaluation was defined as the complex process of determining significance or value of the identified hazards and estimated risks to those concerned with or affected by the decision.* Evaluation included the study of trade-offs between perceived risks and benefits. Risk management was defined as the making of decisions concerning risk and their implementation, but was applied also to the whole complex process of estimation, evaluation, judging acceptability of risks, developing decision strategies, taking account of public opinion on risks and costs of controls, making decisions and implementing risk regulations and other controls.

Davies (1984), in a publication by the Chemical Manufacturers Association, defined three risk terms: assessment, management, and control. Assessment means the process of determining the adverse consequences that may result from the use of a technology or some other action, i.e., estimation of the probability of a hazard materializing; determination of the types of hazard posed; and estimation of the number of people (or things) likely to be exposed and the number likely to suffer adverse consequences. Risk assessments were viewed as useful for establishing priorities for research, for informing the public, and for regulatory considerations. Risk management was defined to encompass all activities involved in actually doing something about a risk, i.e., deciding whether or not to take action; deciding which actions to take; implementing selected actions; and evaluating their effects. Risk control was defined as the overall process for dealing with risk -- priority setting, assessment, and management. In the same publication, Park and Snee (1984) described risk assessment as consisting of hazard identification, hazard evaluation, and risk evaluation. They also equated risk management with regulatory response (including evaluation of benefits of the chemical versus the risks, costs, and alternatives), while Smith (1984) described risk management more succinctly as "the control of exposure to levels where perceived risks are acceptable."

The Office of Science and Technology Policy, in its review of the framework for regulating carcinogens (OSTP, 1985), considered "risk" to be composed of two aspects, hazard (the toxicity of the substance) and exposure (the amount of the substance that people come in contact with); the "risk" in quantitative risk assessment is estimated by coupling the results of the hazard and exposure assessments. (The phrases "hazard evaluation," "the source of hazard," "harzard data," and "toxicity data" are also used in the text.)

A report commissioned by the U.S. Food and Drug Administration by one National Research Council committee (chaired by Stallones) (NRC, 1983), also addressed terminology. This committee had as one objective to assess the merits of separating the analytic functions of developing risk assessments from the regulatory functions of making policy decisions. The report has been favorably received by some other government agencies, including the EPA (EPA, 1984a-1984d) and the Office of Science and Technology Policy (OSTP, 1985), but its terminology was not unequivocally accepted by a prestigious Task Force on Health Risk Assessment of the U.S. Department of Health and Human Services (USDHHS, 1986) or by numerous other authors. The report described risk assessment as "the characterization of the potential adverse health effects of human exposure to environmental hazards" and also as "the use of the factual base to define the health effects of exposure of individuals or populations to hazardous materials and situations. Risk assessment was said to include several elements:

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* Hazards were described as situations that could lead to harm or damage.

- Descriptions of the potential adverse health effects based on an evaluation of results of epidemiologic, chemical, toxicological, and environmental research.
- Extrapolation from those results to predict the type and estimate the extent of health effects in humans under given conditions of exposure.
- Judgments as to the number and characteristics of persons exposed at various intensities and durations.
- Summary judgments on the existence and overall magnitude of the public health problem.

Risk assessment was said to include some or all of the following four steps:

- Hazard identification: The determination of whether a particular chemical is or is not causally linked to particular health effects.
- Dose-response assessment: The determination of the relation between the magnitude of exposure and the probability of occurrence of the health effects in question.
- Exposure assessment: The determination of the extent of human exposure before or after application of regulatory controls.
- Risk characterization: The description of the nature and often the magnitude of human risk, including attendant uncertainty. (The text describes this as an estimation step.)

The NRC committee used the term "risk management" to describe the process of evaluating alternative regulatory actions -- or of weighing policy alternatives -- and selecting among them. The selection process requires the use of value judgments on the acceptability of risk and the reasonableness of the costs of control. It included integrating the results of risk assessment with engineering data and with social, economic, and political concerns to reach a decision.* (The committee also defined a term "risk assessment policy" as consisting of the analytic choices that must be made in a risk assessment, based on both scientific and policy considerations.) This report, one should note, focused primarily on managing the risk assessment process, not on managing risks; it says very little of the latter.

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* This view seems to relegate to the risk management phase all aspects of the identification and scientific quantification of values to be considered.

In contrast, the DHHS task force (USDHHS, 1986) described four major component steps of risk assessment as:

- Hazard identification: The qualitative indication that a substance/condition may adversely affect human health.
- Hazard characterization: The qualitative and quantitative evaluation of the nature of the adverse effects, including their expression as functions of the amount of exposure (dose).
- Exposure characterization: The qualitative and quantitative evaluation of the degree of human exposure likely to occur.
- Risk determination: The integration of these steps into a scientific determination of the level of risk as a basis for policy consideration.

The Task Force noted conceptual differences between its steps and those of the NRC (Stallones) committee:

* The DHHS hazard identification step is the objective qualitative or quantitative determination of a potential hazard, rather than a causal determination of risk:

* The DHHS hazard characterization embraces dose-response assessment, but also includes the determination of differences in risk across subpopulations as well as efforts to characterize by clinical or pharmacokinetic studies the action of the hazard.

* The DHHS risk determination ranges in nature from a binary (risk/no risk) conclusion to a formal, quantitative, multidimensional conclusion complete with sensitivity testing and detailed characterization of uncertainty.

The Task Force felt its model was a more step-wise approach that "make it necessary to consider the results of individual research studies undergirding risk determinations as important contributors to risk assessment more fully and more directly than do the NRC committee and other groups, which have in general chosen to note simply that research precedes risk assessment and provides the scientific basis for this activity." The Task Force also noted typical kinds of information used in these components, as seen in Table A-1.

Finally, a bill introduced in the U.S. Congress to enact a "Risk Assessment and Demonstration Act of 1985" (called the "Ritter Bill") adopted the terminology of the NRC report, but also cited a need for better "comparative risk assessment," which was defined as "a procedure in which the assessment of the risks associated with one course of action and the assessment of risks associated with alternative courses of action are compared and contrasted with each other and with the kinds of risks people normally face in their individual lives" (U.S. Congress, 1985). The terms "comparative risk

TABLE A-1

INFORMATION USED IN ASSESSING HEALTH RISKS ACCORDING TO USDHHS TASK FORCE ON HEALTH RISK ASSESSMENT

(USDHHS, 1986)

1. Hazard Identification
   - a. Human data
     - Monitoring and surveillance (including vital statistics
     - Epidemiologic studies
     - Clinical studies
   - b. Animal data
   - c. In vitro tests
   - d. Molecular structure-activity relationships

2. Hazard Characterization
   - a. Human studies
     - Epidemiologic studies
     - Clinical studies
   - b. Animal studies
     - Minimal effects determination
     - Dose-response modeling
     - Special issues, including interspecies conversion and high to low dose extrapolation
   - c. Pharmacokinetic studies (including physiologic rationale)

3. Exposure Characterization
   - a. Demographic information
   - b. Ecologic analyses
   - c. Monitoring and surveillance systems
     - Animal
     - Human
   - d. Biologic monitoring of high-risk individuals
   - e. Transport modeling (mathematical)
   - f. Integrated exposure assessments
     - Over time
     - Over hazard (synergy)

4. Risk Determination
   - A. Mathematical
     - Unit and population risk estimates
     - Threshold determination (e.g., safety factor approach, no-observed-effect level)
     - Statistical characterization of uncertainty
   - b. Formal decision analysis
   - c. Inter-risk comparisons
   - d. Qualitative - panel reviews
   - e. Qualitative - informal scientific advice
   - f. Risk-benefit analysis

assessment" and "comparative risk-cost-benefit study" were used over a decade ago by Kates (1975) and the Atomic Energy Commission (USAEC, 1974), respectively.

Table II-1 in the text of the report summarizes many of the definitions and distinctions in the terminology in the risk assessment field. Lawless et al. (1984) recently reviewed the terminology used in the risk assessment area and proposed an extensive set of definitions believed to be consistent internally and with the best of current usage.

2. Risk Assessment Under RCRA

The Resource Conservation and Recovery Act of 1976 (as amended through November 1984) is less specific about the need to determine the reasonableness of risks or to perform risk assessments than are some other environmental and consumer protection laws, such as the Toxic Substances Control Act, the Federal Insecticide Fungicide and Rodenticide Act, and the Consumer Product Safety Act. Nevertheless the RCRA language clearly implies that risks will need to be studied in some cases.

For example, RCRA defines hazardous waste as "a solid or combination of solid wastes which, because of its quantity, concentration or physical, chemical or infectious characteristics may: (a) cause or significantly contribute to an increase in mortality or to an increase in serious irreversible or incapacitating reversible illness; or (b) pose a substantial present or potential hazard* to human health or the environment when improperly treated, stored, transported, disposed of, or otherwise mismanaged."

Sec. 3013 of RCRA, "Monitoring, Analysis, and Testing," addresses the issue of risk indirectly. It states that upon receiving information that the presence or release of hazardous waste at a treatment, storage, or disposal facility (TSDF) may present a substantial hazard to human health or the environment, the EPA Administrator can require that the owner/operator of the site conduct monitoring, testing and analysis to determine the nature and extent of such hazard.

Sec. 3019, "Exposure Information and Health Assessments" (added in the 1984 amendments), speaks most directly to risk assessment needs. 'Health Assessments' are defined to "include preliminary assessments of the potential risk to human health posed by individual sites and facilities subject to this section, based on such factors as the nature and extent of contamination, the existence of potential for pathways of human exposure (including ground or surface water contamination, air emisions, and food chain contamination), the size and potential susceptibility of the community within the likely pathways of exposure, the comparison of expected human exposure levels to the short-term and long-term health effects associated with identified contaminants and any available recommended exposure or tolerance limits for such contaminants, and the comparison of existing morbidity and mortality data on diseases that may be associated with the observed levels of exposure." The definition continues: "The Assessment shall include an evaluation of the risks to the potentially affected population from all sources of such contaminants, including known point or nonpoint sources other than the site or facility in question. A purpose of such preliminary assessments shall be to help determine whether full-scale health or epidemiological studies and medical evaluations of exposed populations shall be undertaken."

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* RCRA does not define 'hazard,' but as used here to define 'hazardous waste' it appears to be essentially synonomous with conventional definitions of 'risk.'

This section provides that issuance of permits for operation of a landfill or surface impoundment shall be dependent upon submission by the owner/operator of certain information related to the potential for exposure of the public to the hazardous waste constituents. This submission shall include information on potential releases, environmental pathways, and nature and magnitude of human exposure. This section also provides that the Administrator or states with authorized RCRA programs shall make this information available to the Agency for Toxic Substances and Disease Registry (as established by the Comprehensive Environmental Response, Compensation and Liability Act of 1980). It further provides that the Administrator (or said states) may request that Agency to conduct a health assessment of any landfill or surface impoundment if (in the Administrator's judgment) it "poses a substantial potential risk to human health, due to the existence of releases of hazardous constituents, the magnitude of contamination with hazardous constituents which may be the result of a release, or the magnitude of the population exposed to such release or contamination." Finally this section provides that priority in conducting health assessments shall be given "to those facilities or sites for which: there is documented evidence of release of hazardous constituents; the potential risk to human health appears highest; and existing health data are deemed inadequate to assess the potential risk to human health."

3. Useful Definitions

A set of definitions of terms used in the risk assessment and health effects fields are presented here for the convenience of the reader.

Hazard--A source of a threat or danger, often implying major natural or man-made (especially technological) dangers, or dangers involving substantial elements of chance or accident; may refer to specific substances, objects, or activities that have characteristics (such as inherent toxic, energetic, or gravitational aspects) that cause them to be considered sources of danger; sometimes used (popularly) as a synonym for "danger" or "risk."

Probability--The possibility, likelihood, or frequency that an activity, event, or outcome will occur. A measure of chance. Classical or objective probability is defined as the ratio of the number of times a given outcome occurs to the total number of possible outcomes. Subjective probability derives from a view of probability as a rational degree of confidence or belief: subjective weights are assigned (according to certain theoretical principles) to possible outcomes of an action, so that an operationally meaningful analysis can be performed. A statement of probability is value-neutral. It does not imply that a stated consequence is beneficial or adverse; that is determined by the individual evaluator.

Risk--(noun) is an expression of the uncertain potential of incurring a specified adverse consequence (e.g., death) during some stated measure of interval (e.g., years, million miles, hundred skydives, etc.). All expressions of risk are conditional. Risk may be usefully expressed either quantitatively or qualitatively:

- A quantitative statement of the probability of occurrence of a defined adverse effect, based on substantial amounts of the required kinds of information and data. A statement of risk as a probability has meaning only if one states the units of measure and the conditions applicable.
- A qualitative statement of the likelihood or possibility of occurrence of one or more identified adverse effects, based on partial or minimal information or historical perspective.

Risk combines the concepts of future chance, the loss of something of value, and a standardized measurement parameter (such as time or other numerical measure). It involves a statement of this chance in the absence of complete information, in qualitative or quantitative terms (frequently as a probability). Popular usage commonly refers to the "loss side" of a simple wager or business venture.

Exposure to risk--An act or condition of being exposed or open to a given threat from a given source (e.g., pathogenic organisms, toxic chemicals, radiation, safety hazards, or economic changes) that could cause adverse consequences.

Exposure to pollutants--Exposure occurs at the point in space and time at which the toxic substance is present at the interface between the environment and a biological organism.

Exposure assessment--This term lacks a widely accepted definition. It is often used to describe different sets of activities by researchers with different viewpoints. Some researchers consider exposure assessment to begin with chemical analysis of the contaminants in the air, water, food, surfaces, etc., which people actually inhale, ingest, touch, etc. By knowing concentrations and assuming the daily volume of air breathed, tapwater consumed, etc., the exposure rate and exposure dose over a given duration can be estimated for each exposed individual. The exposure assessment is usually completed by quantifying the known or assumed population at risk. Other researchers place greater emphasis on analyzing or modeling the transport and interactions of chemical substances from the point at which they enter the environment through air, water, land, and ecosystems until they reach receptor populations, i.e., they quantify the concentrations of toxicants at the points in space and time where they intercept populations, and they predict the extents of exposures that result. Still other researchers may begin the exposure assessment with qualitative and quantitative analyses of the entry of contaminants into the environment, i.e., with an assessment of the sources. Hushon and Clerman (1981) divided exposure assessment into five steps: chemical description; materials balance; pathways of environmental release; population profiles; and "assessment" in which the environmental concentrations and population profiles are combined to give exposure profiles. In one Office of Technology Assessment report, the scope of exposure assessment was extended to include absorption within the organism and transport to the site of toxic activity (OTA, 1984).

Risk estimation--A quantification component of the risk assessment process in which one estimates the probabilities of occurrence of explicit adverse consequences and the extent of the consequences. The estimates may be made by formal analysis of an existing data base in order to minimize subjectivity or by judgmental analysis based on experience, perception, and intuition.

Risk determination--A part of the risk estimation process, frequently implies a proactive collection of experimental or statistical data that can be used to increase the confidence of estimated risk factors. (It may, at times, refer to a process of analyzing risk factor data to reach a consensus for decision purposes, e.g., judicial decisions.)

Risk evaluation--The complex process of assigning individual and societal values to identified possible adverse consequences of a proposed action or decision. An individual may evaluate risks either consciously or subconsciously depending on the situation. Different individuals may value the same possible consequence quite differently, depending on their personal value systems, and a given individual may assign different values at different times as his or her values change. Society may evaluate risks formally or informally. Different segments within a society or different societies may value the same consequence quite differently, and societal values also change over time and generations. The accuracy of the risk evaluation step is frequently a major point of contention in the risk assessment and decision making processes. Consequences may be divided into values that are or can be readily monetized (e.g., economic losses) and values that usually are not monetized except under certain demanding conditions (e.g., awards for personal injury, loss of life, or environmental damage in the settlement of legal suits).

Risk analysis--A general term that includes such activities as risk estimation and evaluation (particularly those aspects reducible to mathematical expression) pertaining to the adverse consequence of a proposed action. Risk analysis does not include extensive considerations of the anticipated benefits, except the benefit of risk reduction. Note, however, that some authors use the terms risk analysis and risk assessment synonymously.

Risk assessment--The broad process of identifying, characterizing, quantifying, and evaluating the risk, cost, and benefit factors that are associated with a proposed action or contemplated decision. It usually implies an effort to determine the balance of known and estimated benefits, costs, and risks, in which careful attention has been given to potentially external costs and inequitable societal risks, so that a socially acceptable decision can be reached. Note, however, that some authors and some governmental groups have used this term in a more restricted sense (see risk analysis) and have proposed various definitions of qualitative, quantitative, and probabilistic risk assessment.

Comparative risk assessment--A systematic, multidimensional process for objectively organizing, analyzing, evaluating, and placing in perspective information about the risks, costs, and benefits of technological alternatives (particularly to human health, safety, and the environment), as an aid to public policy decision making in the management of risks under uncertainty. Comparative risk assessment is less mathematically oriented than some related activities (e.g., risk estimation from toxicity and exposure data) and less mechanistic than some others often are (e.g., benefit-cost analysis). It emphasizes identification and evaluation of trade-offs rather than optimization of a single value.

Risk management--A range of individual and social actions taken to avoid, minimize, reduce, limit, or otherwise control the degree of exposure to risk situations or the magnitude of adverse consequences. It includes at times actions designed to maximize benefits at a given level of risk. Risk management approaches include risk aversion steps, social controls, behavior modifications, engineering controls, administrative controls (such as required work practices, personal protection, education and training, medical surveillance, and record keeping), and risk distribution.

Uncertainty--A statement of the degree to which a system, process, or measurement, or the components thereof are clearly identified or defined, or that an event is believed sure to occur.

Uncertainty analysis--A procedure for attempting to quantify a statement of uncertainty, e.g., quantification of the uncertainty associated with an estimate of the number of cases of a specific adverse human health effect for a given waste management practice.

Uncertainty factor--A measure of the uncertainty range associated with a point risk estimate. The term has also been used synonomously for safety factor (a risk management concept).

Dose--A measure of the amount of test substance or radiant energy a test subject is given. The dose may be stated in terms of weight or concentration in a medium of the substance. Administered dose is the amount the subject receives. Effective dose usually means the concentration at the target site, but is sometimes used to mean a threshold dose, i.e., the minimum dose required to produce a specified response. Environmental dose is the amount of an environmental pollutant that actually contacts or enters the organism through bodily membranes and portals: intact or broken skin, eyes, nose, and mouth. It is analogous to the administered dose in a controlled toxicological study.

Carcinogenicity--The property of causing the formation of tumors, new growths of tissue serving no useful function. In some usages the term carcinogenicity is restricted to malignant tumors (those with a potential for unlimited growth by expansion or by metastasis, i.e., sending out "daughters" to grow in other locations), with the term oncogenicity used for all tumors. The potential for tumor expansion (malignancy or nonmalignancy) is often difficult to determine in animal studies and conclusions are sometimes controversial. Therefore the term carcinogenicity is often used in the unrestricted sense unless specifically limited.

Teratogenicity--The property of causing physical defects in a developing embryo of an unborn offspring. These defects (split palate and hare lip are among the more common ones in humans) are not inheritable. (Note that mutagenicity refers to inheritable defects.) Teratogenic chemicals usually exhibit their effects following exposure of the female during a specific stage in early pregnancy.

Embryolethality--The property of causing the death of a developing embryo. It may result from severe teratogenicity, from mutagenicity, or from an adverse effect on the mother. Regardless of the cause, the result is a nonviable mother-embryo relationship followed by the resorption of the embryo.

Dermatotoxicity--Refers to toxic effects, normally visible lesions, on the skin. They may result from local application (such as a rash from contacting poison ivy) or from ingestion, inhalation, or other intake followed by distribution throughout the body by the blood.

Hepatotoxicity--Refers to toxic effects on the liver. They may be physical lesions, detected by microscopic examination of liver tissue, but are more commonly biochemical lesions, detected by the abnormal concentration of one or more chemicals in body fluids (blood or urine) or tissues. Jaundice, a yellowish pigmentation of the skin, other tissues, and body fluids, is an extreme, readily visible example of a biochemical lesion.

Nephrotoxicity--Refers to toxic effects on the kidney. They may be physical lesions or functional lesions, and are detectable by analysis of the urine.

Neurotoxicity--Refers to toxic effects on the nervous tissue, including both the central nervous system (brain and spinal cord) and the peripheral nervous system. Neurotoxic effects vary widely. Some are readily observable, e.g., tremors (trembling, shivering, shaking) or convulsions. Others such as abnormal reflexes or coordination difficulties require testing for their detection (e.g., inability to walk a straight line or to touch one's fingertip to nose with the eyes closed, both elements of a "field sobriety test" for the neurotoxic effects of ethanol).

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APPENDIX B

DEVELOPMENT OF SCENARIOS FOR COMPARATIVE RISK ASSESSMENT OF HAZARDOUS WASTE MANAGEMENT

The development and use of realistic scenarios can enhance studies of the potential consequences of alternative decisions and actions. In a recent comparative risk assessment of hazardous waste management strategies, Midwest Research Institute developed and used detailed scenarios in the analysis of alternative management approaches for selected wastes.[1] The scenarios were intended to be as representative as possible of the range of existing practices involving these wastes. Development of the scenarios gave many insights into the scenario construction process. This appendix presents guidelines that can be applied to the development of scenarios for other wastes and waste management practices for comparative risk assessments.

Before scenarios can be developed, one or more specific hazardous wastes must be selected for analysis. Different selection mechanisms and criteria can be adopted, depending on the goals and management plan for each study. Wastes may be selected to be representative of several diverse factors, including: sources; quantities; chemical, physical, and biological properties; and waste management practices. In some cases, high priority may be placed on selecting a waste that is representative of a specific class of wastes, or on the availability of data. Alternatively, a screening process may be applied to many or all listed hazardous wastes to identify those to be subjected to detailed analyses. A list of candidate hazardous wastes, designated by source industry, process, or other descriptors, can be screened according to the desired criteria, and one or more wastes can then be selected for assessment.

Assuming that the hazardous waste has been selected, the process for development of scenarios can be described in five steps:

1. Characterize existing waste sources
2. Select waste management alternatives for evaluation
3. Select model waste source and disposal sites
4. Define waste generation scenario
5. Define waste disposal scenarios

Each of these steps is discussed below, and illustrated in part with examples from the earlier study.[1]

1. CHARACTERIZE EXISTING WASTE GENERATION SOURCES

This step requires the collection, review, and evaluation of information on the technoeconomic aspects of the waste generation source. This may include information on: the industry or other source that generates the waste; the locations of the sources; the products and processes that yield wastes; the quantity and form of waste generated; and the treatment and disposal practices in use. This information provides the basis for developing composite, model, or representative disposal facilities for comparative risk assessment.

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[1] Midwest Research Institute, "Comparison of Risks and Costs of Hazardous Waste Alternatives: Methods Development and Pilot Studies," Draft Final Report prepared under EPA Contract No. 689-01-6558, Subcontract No. 130.155, November 19, 1984.

Information for this step will be obtained from several sources, including: EPA documents (e.g., hazardous waste listing documents, and any pertinent industry/waste assessment reports); industry and trade sources (e.g., delisting requests; personal contacts); and the published literature (e.g., the Kirk-Othmer Encyclopedia of Chemical Technology; trade association reports; trade journals, etc.). The characterization should address at least the following specific factors.

1.1 Source Locations

The number and locations of domestic sites at which the designated waste is generated are determined first. These are often the sites for manufacturing one or more products for which the waste is a by-product. For industrial sources of the waste, characterize the quantity of product manufactured by industry, company, and site. Table B-1 illustrates the nature and level of detail given in a study of carbon tetrachloride production wastes.[1] Note if the distribution of plant capacities is fairly normal or highly skewed since this will be an important consideration in defining a model plant. Note also the physical characteristics of the sites of these sources for use in site selection for the model source. Recent or proposed changes (e.g., mentioned in the trade literature or other market analyses) of the number or location of existing sites should also be considered in selection of model sites, products, or processes.

1.2 Source Processes

Identify the processes in use at the sites where the wastes are generated. Note the range of process parameters in use in the industry and impacts that these may have on generation of waste. Identify point sources of waste generated or released within the manufacturing process. Collect information on the flow of materials in the process and waste streams. One or more materials flow diagrams typical of the industry processes will be useful. Figure B-1 illustrates such a diagram for chlor-alkali manufacture using mercury cell electrolysis, in which mercury-contaminated brine muds are the hazardous waste to be disposed.[1] Note any pretreatments of raw materials, unusual early-stage processing steps or recycling steps that may be used by some industry members to reduce or modify the waste that is generated. Note also any reported trends in the processes used by the industry that could substantially affect the quantity or nature of the waste. All of this information will be important in defining a model waste generation scenario.

1.3 Waste Quantities and Compositions

Characterize the hazardous wastes being generated at each kind of point source by quantity and composition. Identify the quantities both in relative

TABLE B-1

ILLUSTRATIVE ANALYSIS TO IDENTIFY WASTE SOURCES: CARBON TETRACHLORIDE PRODUCTION WASTES

Company	1983 Nameplate Capacity, MT (10^6 lb)	Type of Process or Coproduct	Waste Constituents Predicted in Heavy Ends
Dow Chemical USA			
Pittsburg, California	36,288 (80)	Chlorination of methane, perchloroethylene coproduct	A
Plaquemine, Louisiana	56,700 (125)	Chlorination of methane	A
E. I. du Pont de Nemours and Company, Inc.			
Corpus Christi, Texas	136,080 (300)	Perchloroethylene coproduct	B
LCP Chemicals & Plastics, Inc.			
Moundsville, West Virginia	4,536 (10)	Chlorination of methane	A
Stauffer Chemical Company			
Le Moyne, Alabama	95,256 (210)	Chlorination of carbon disulfide	C
Vulcan Materials Company			
Geismar, Louisiana	40,824 (90)	Chlorination of ethylene, perchloroethylene coproduct	D
Wichita, Kansas	27,216 (60)	Chlorination of ethylene, perchloroethylene coproduct	D
Total	396,900 (875)		

Source: Reference 1.

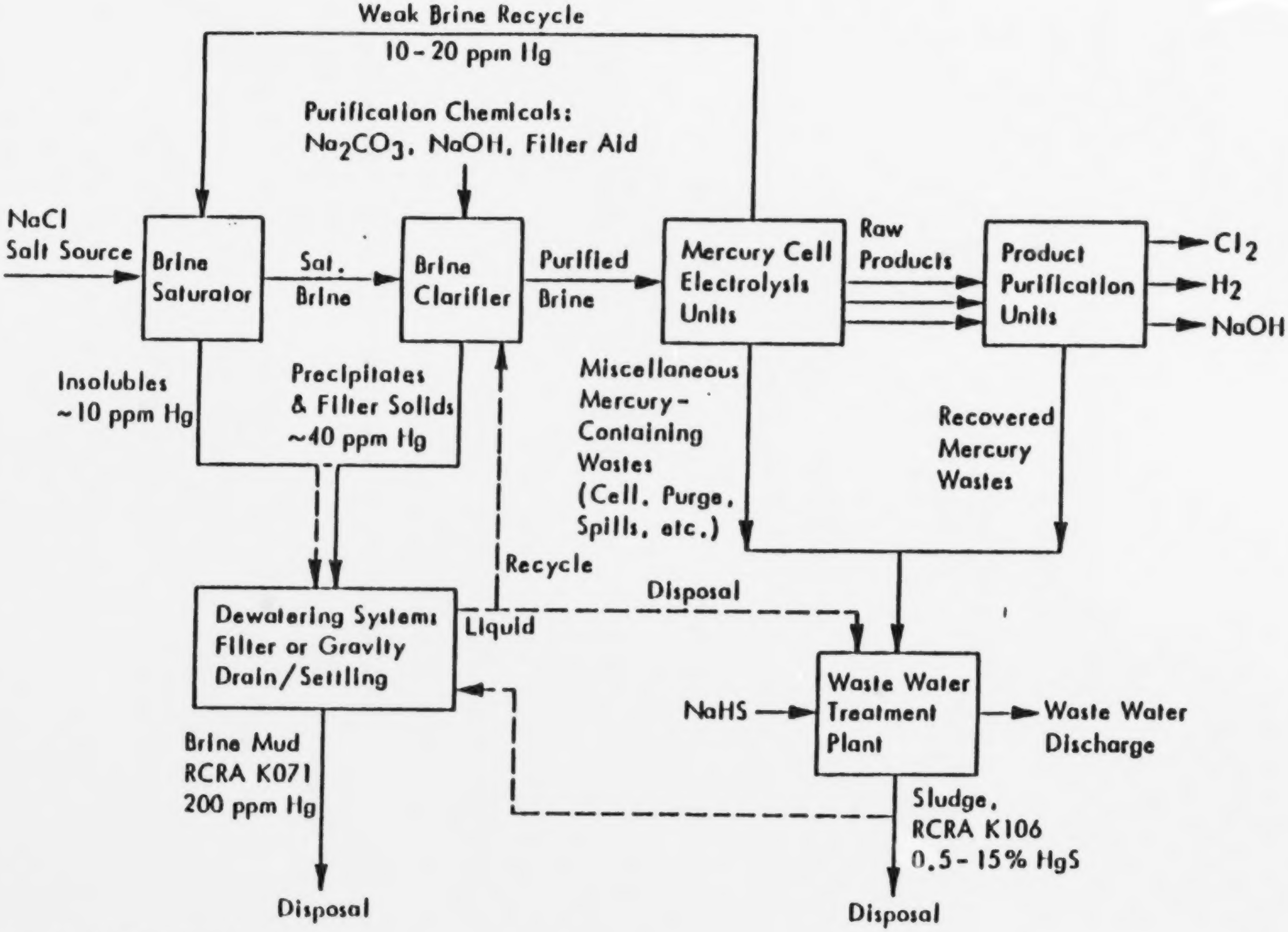
[a] Major waste constituents by type of process:

A. Chlorination of methane: Hexachloroethane, hexachlorobutadiene, perchloroethylene, carbon tetrachloride.

B. Chlorinolysis of hydrocarbon feedstocks: Hexachloroethane, hexachlorobutadiene, perchloroethylene, hexachlorobenzene, carbon tetrachloride.

C. Chlorination of carbon disulfide: This process would be waste-free if properly operating; otherwise, sulfur monochloride and carbon tetrachloride would be present.

D. Chlorination of ethylene: Hexachloroethane, perchloroethylene, hexachlorobutadiene, hexachlorobenzene, carbon tetrachloride.


Weak Brine Recycle
10 - 20 ppm Hg
Purification Chemicals:
Na_2CO_3, NaOH, Filter Aid
NaCl
Salt Source
Brine Saturator
Sat.
Brine
Brine Clarifier
Purified
Brine
Mercury Cell Electrolysis Units
Raw
Products
Product Purification Units
Cl_2
H_2
NaOH
Insolubles
~10 ppm Hg
Precipitates
& Filter Solids
~40 ppm Hg
Miscellaneous
Mercury-
Containing
Wastes
(Cell, Purge,
Spills, etc.)
Recovered
Mercury
Wastes
Recycle
Disposal
Liquid
Dewatering Systems
Filter or Gravity
Drain/Settling
NaHS
Waste Water Treatment Plant
Waste Water
Discharge
Brine Mud
RCRA K071
200 ppm Hg
Sludge,
RCRA K106
0.5 - 15% HgS
Disposal
Disposal

Source: Reference 1.

Figure B-1 - Typical Brine Mud Generation and Treatment Process in Chlor-Alkali Manufacture terms (e.g., tons per kiloton of product manufactured) and in absolute terms (e.g., tons per year at each site), because this information will be useful in defining a model plant. Note both the average and the range of the amount of waste. Identify the range of variation both within and across sites, if possible. The waste must be characterized in terms of the chemical constituent or properties that caused the waste to be classified as hazardous. Record the concentration of the identified hazardous constituent(s) in the waste and its properties. Record the physical form and properties of the waste (e.g., solid, liquid, or slurry; volatility). Note also other constituents that may affect the environmental release, transport, or impacts of the constituent(s) of primary concern. Characterize both average composition and the variation across sites and process variables. This information will be needed in defining a model waste.

1.4 Waste Pretreatments

Applicable pretreatment processes must be characterized. These processes can be an internal step in the manufacturing operation or a subsequent step in preparation for transport, storage, or disposal. Such processes may include the use of additives, filtration, centrifugation, gravity settling, etc. Note the effects that such treatments have on the waste quantity, properties, or composition. This information will also be useful in defining a model waste that is as representative as possible of the industry or other source.

2. SELECT WASTE MANAGEMENT ALTERNATIVES FOR EVALUATION

Several waste management practices (or variations) generally can be identified for each hazardous waste. From these, select two or more of the most viable alternatives (three to five may be optimum) for the comparative assessment. Practices should be identified on the basis that individually they are realistic for the subject wastes and that collectively they include a substantial range of existing or proposed approaches. Normally all of the selected alternatives would meet the requirements of current or forthcoming environmental regulations, although one that illustrates current practice provides a useful baseline case for comparison, even if it does not meet the standards.

Selected practices usually would involve changes in treatment, storage, transportation, or disposal technologies, and could include variation in the pretreatment or process practices (e.g., to minimize contamination of the waste with hazardous constituents or reduce the quantity of waste generated). A partial list of possible technologies is shown in Table B-2. Viable alternatives must be technically feasible, compatible with the waste to be disposed, defensible under stated regulatory assumptions, and economically worthy of analysis under those assumptions. The alternative most likely to be least costly while meeting expected regulations should be included if it can be identified. Specific properties of the designated wastes must be considered so that the assessment compares realistic scenarios (e.g., incineration would probably be excluded for a waste that contained high concentrations of a volatile toxic element such as mercury or arsenic).

TABLE B-2

ILLUSTRATIVE WASTE MANAGEMENT TECHNOLOGIES FOR COMPARATIVE RISK ASSESSMENTS

- Pretreatment
- Landfill on-site or off-site
- Special design landfills
- Dewater waste and landfill on-site or off-site
- Aqueous solvent extraction, treatment of extract, and landfill of residue on-site
- Stabilization and landfill on-site or off-site
- Surface disposal impoundment on-site
- Incineration on-site, off-site, or at-sea
- Solvent extraction, incineration of extract, and residue landfill on-site
- Recycle to process
- Use as feedstock for manufacture of other products
- Process changes to alter quality or quantity of waste

Source: MRI.

Each of the selected waste management practices should be identified with a convenient descriptive title. One of the practices usually should be designated as the baseline. Disposal in a RCRA-approved landfill may be a generally useful base case.

3. SELECT MODEL WASTE SOURCE AND DISPOSAL SITES

Now that the selected hazardous waste, its source, and selected management practices have been identified and characterized, the next step is to choose one or more specific geographic site(s) for a model source of Table B-2 the waste (e.g., a model plant, an abandoned disposal site, or a contaminated area). The selected site(s) may be chosen to reflect closely the locations of one or more existing sites. Alternatively, it might be chosen to be as representative as possible of most of (or a subset of) all the existing sites, or it may be selected by other stated criteria. For wastes that are generated and disposed at only one or a few similar sites, the selected model site can reflect reality very closely. In fact, many wastes are known to go to fewer than 10 sites; then all real sites could be analyzed, if desired. The wastes that go to many sites can be grouped sometimes in such a way that only a few highly representative model sites are needed. For other wastes, however, substantial site diversity exists and the selection process will be more difficult. In general, this step will require several actions:

* Identify geographical areas as potential locations (e.g., state and county or city) for the model production-waste generation and disposal facilities. Normally these would be representative of the industry or source, or of specific waste management problems. Candidate locations must be compatible with the waste management practices selected for assessment. Different waste management practices may require different disposal sites (e.g., landfill versus incineration at sea).

* Review and characterize quantity and quality of information and data available for these representative general locations. Note information and data on environmental parameters (e.g., temperature; rainfall; evaporation; wind speed and direction (range and average); soil and subsurface structure and porosity; groundwater depth, direction of flow, and velocity of flow. Note population and land use distributions (including ecological aspects) at representative general sites. Identify possible specific sites in each area that are representative of the industry or source. Compare availability of information and data for alternative sites. Sites for which available data are inadequate may be eliminated, unless other considerations are overriding. For example, one may wish not to eliminate the most representative site. In such cases, special efforts may be required to gather or estimate necessary data.

* Select site(s) according to the criteria previously stated for the study. In general, one could select sites which best combine representativeness of the industry and adequacy of data bases for the environmental transport and population at risk.

- Develop detailed information on the meteorological and hydrogeological conditions at each generation site and at sites involved in treatment, transportation, storage, or disposal activities. Table B-3 illustrates the kind of information developed for a study of the disposal of carbon tetrachloride production wastes.[1]

- Develop population distribution data and information for all selected sites for subsequent use in developing detailed waste generation and disposal scenarios.

4. DEFINE WASTE GENERATION SCENARIO

Based on the information used to select the hazardous waste and information on its source in Step 1, develop a scenario for a model waste source at the site(s) selected above. The scenario should specify the manufacturing process and production levels (this would not apply in clean-up of an abandoned hazardous waste site). An overall materials flow diagram should be prepared that quantifies the inputs and outputs (as shown previously in Figure B-1 for chlor-alkali manufacture). Waste generation parameters should be defined; they may be defined to be as representative as possible of the industry (e.g., average values) or to illustrate specific situations. The quantity and composition of the waste should be stated. Point sources of waste generation within an industrial process should be identified. Any pretreatments used for the wastes should be noted.

An illustration of the geographical setting and spatial relationships for the waste generation and disposal sites will be helpful. Figure B-2 shows a hypothetical setting for a model chlor-alkali plant.[1]

The time period over which the waste is generated and disposed must be explicitly stated for analysis.* A 20-year generation period may be reasonable for most wastes, but longer or shorter periods may be preferable in some assessments (e.g., only 6 months was appropriate for the clean-up of dioxin-contaminated soil).[1]

5. DEFINE WASTE DISPOSAL SCENARIOS

Based on the selection of waste management practices in Step 2, model source and disposal sites in Step 3, and the detailed waste generation scenario defined in Step 4, detailed scenarios are developed for the treatment, storage, transportation, and disposal of the wastes as appropriate for each alternative waste management practice. These scenarios must be realistic, like the waste generation scenarios, and representative of existing or proposed practices so that the results of the subsequent assessment may be

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* A time period will also have to be selected over which post-disposal effects will be analyzed in the overall comparative risk assessment.

TABLE B-3

ILLUSTRATIVE PHYSICAL CHARACTERIZATION OF LAND DISPOSAL SITE FOR CCl_4 PRODUCTION WASTES

Plant Location

Southern Texas, Brazoria County, northwest of Freeport, latitude 28°58'9"N; longitude 95°23'20"W; near the Brazos River.

Terrain

Flat coastal plain

Soil

Norwood silt loam soil; silt loam averages 0.3% slope (0 to 1% range); is well drained; rarely flooded; has slow surface runoff; and moderate permeability (1.5 to 5.1 cm/hr)

Average Annual Rainfall

130 cm (52 in.)

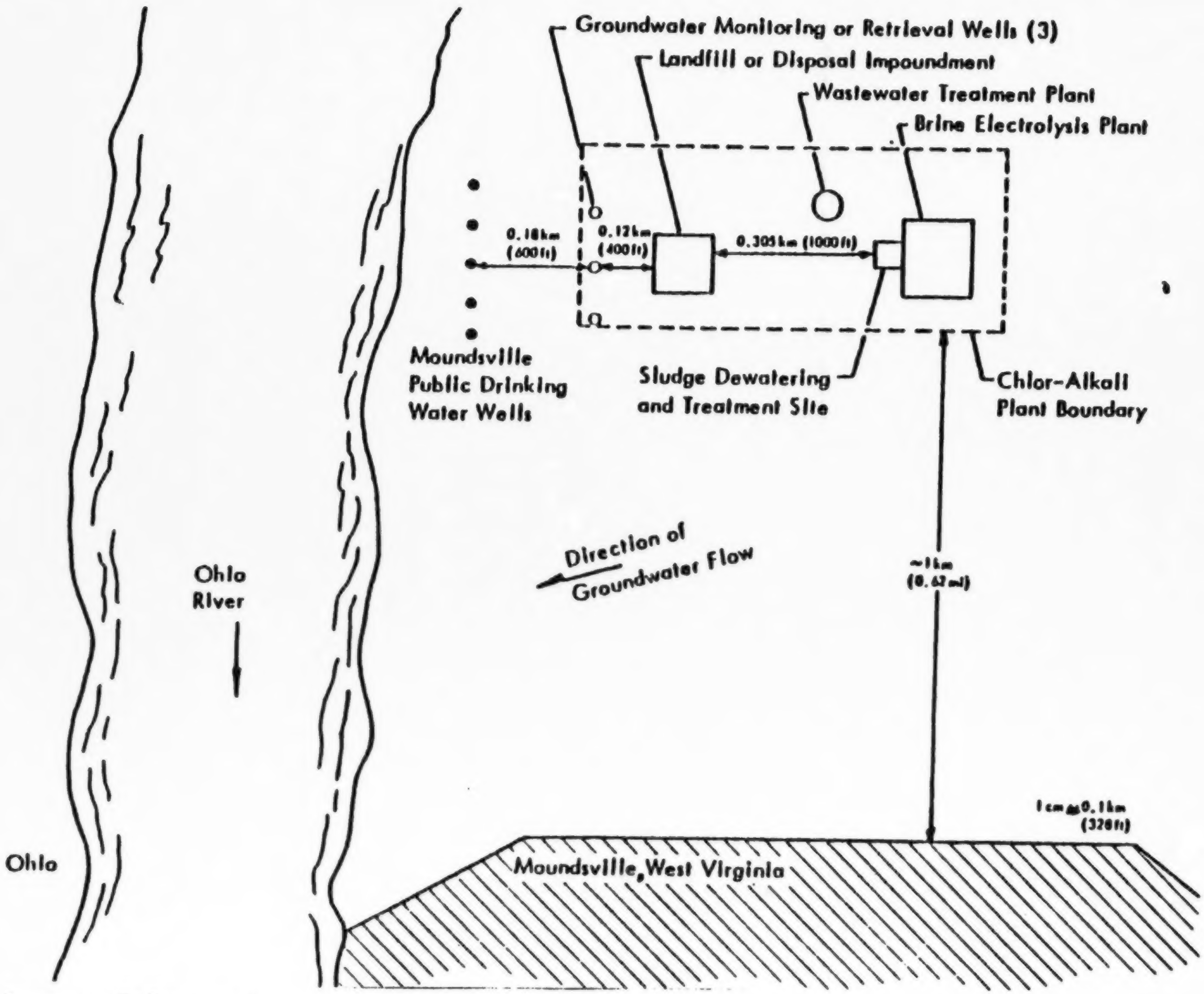
Net Evapotranspiration

10.2 cm (4 in.)

Hydrogeology

Beneath surface silt soil is the Beaumont clay; 53 m thick at the site; permeability assumed to be 10^{-7} cm/sec. Beneath the Beaumont clay is the upper unit of the Chicot aquifer; consists of interconnected sands; thickness at the site is 14 m. Groundwater at the site is under artesian conditions; therefore, water level in a well is 13.7 m (45 ft) below datum (ground surface).

Source: Adapted from Reference 1.



Groundwater Monitoring or Retrieval Wells (3)
Landfill or Disposal Impoundment
Wastewater Treatment Plant
Brine Electrolysis Plant
0.18km (600ft)
0.12km (400ft)
0.305km (1000ft)
Moundsville Public Drinking Water Wells
Sludge Dewatering and Treatment Site
Chlor-Alkali Plant Boundary
Direction of Groundwater Flow
Ohio River
~1km (0.62mi)
1cm≈0.1km (328ft)
Ohio
Moundsville, West Virginia

Source: Reference 1.

Figure B-2 - Hypothetical Site of Chlor-Alkali Plant and Brine Mud Disposal Facility unbiased and as broadly applicable as possible. All scenarios for a given waste should be consistent in terms of duration (e.g., 20 years each) and quantities of waste generated and disposed.

Information for the waste disposal scenarios may be obtained from several sources, including: minimum requirements of existing regulations; documentation supplied by waste source industry; manufacturers of technology in use or available for waste disposal; hydrogeological data for representative disposal sites; and engineering judgment. All parameters of the waste disposal practices should be defined explicitly. A number of such parameters for the landfill of carbon tetrachloride production wastes are shown in Table B-4.[1] Quantities of chemicals or additives mixed with the waste and equipment for mixing the waste should be identified. Loading/ unloading practices, transfer or transporting equipment at all stages, and vehicle routes and distances should be specified. A materials flow diagram of the disposal process is helpful, and can also indicate points of potential release of contaminants to the environment. Figure B-3 provides a sample flow diagram for carbon tetrachloride production waste disposal in an off-site landfill.[1] Techniques incorporated in each alternative to monitor or control losses to the environment should be stated and characterized.

Remedial or corrective action plans (e.g., spill cleanup; pumping of contaminated groundwater) may be stated as part of the disposal scenario, or perhaps more clearly as a separate subscenario. Scenarios for corrective action must be developed where deemed appropriate for each waste management scenario. Corrective action scenarios may give particular attention to the retrieval of contaminated groundwater, and should include consideration of response to such problems as spills to surface waters. Assumptions concerning the temporal aspects of corrective action should be stated explicitly. These may include future effectiveness of leak detection, available technologies, and societal requirements. Corrective groundwater retrieval action might not be completely effective; the analyst might wish to make an explicit assumption that reflects this possibility. (An assumption of 100% effectiveness may reduce estimated adverse health effects to zero for all waste management alternatives, and therefore reduce the comparative analysis to a consideration of costs alone.) The use of a range of effectiveness may also be considered as part of the uncertainty analysis.

SUMMARY AND COMMENT: The performance of valid comparative risk assessments for technology-related decisions requires the development of realistic scenarios for alternative approaches. The five-step process described above should be a useful approach for development of scenarios for hazardous waste management decisions.

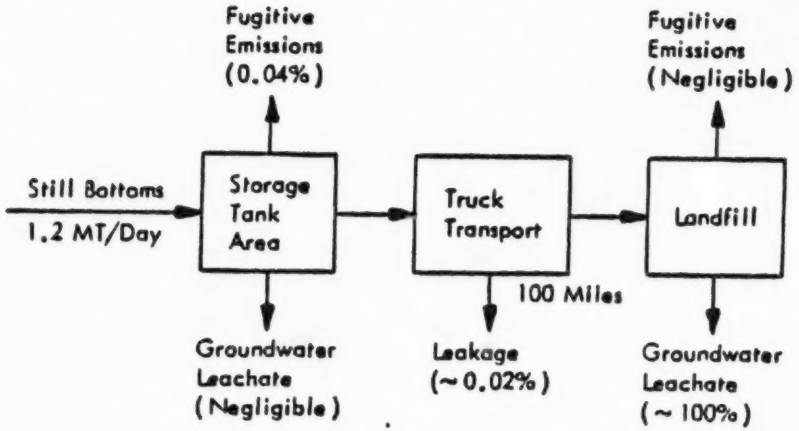
Requirements of time, effort, and data are substantial for development of the most useful scenarios. For many decisions, time and resources may preclude a comprehensive assessment of alternatives, or data limitations may limit the cost effectiveness of highly detailed assessments. Elements of the present guidelines still should help in developing a systematic analysis. In some cases, the appropriate decision may be clear after a less comprehensive assessment of less detailed scenarios than described herein. In cases in which such a preliminary analysis does not point clearly to a decision, it may

TABLE B-4

ILLUSTRATIVE DESIGN OF LANDFILL WITH A SINGLE SYNTHETIC LINER

Landfill Feature	Description
Size of landfill	1,742 m^2 by 3.7 m deep
Containment system	Geotextile 0.30 m sand layer 36 mil Hypalon liner 0.15 m sand layer
Synthetic liner permeability	1×10^{-12} cm/sec
Leachate collection and removal system	Drainage tiles (spaced 15.25 m apart) Gravel Sump and pump Main pipe
Leak detection system	None
Final cover	0.61 m vegetated layer Geotextile 0.30 m sand layer 20 mil synthetic liner 0.61 m clay layer Slope = 3%
Groundwater monitoring	Three wells 122 m down-gradient spaced 122 m apart and one well 122 m up-gradient
Recovery wells	Three wells 122 m down-gradient spaced 122 m apart, fully penetrating the saturated zone, cased, screened the width of the water bearing stratum, and gravel packed.
Recovery pumping rates	76, 379, and 757 L/min assumed for each well to determine contaminant recovery efficiency

Source: Reference 1.


Fugitive Emissions (0.04%)
Fugitive Emissions (Negligible)
Still Bottoms
1.2 MT/Day
Storage Tank Area
Truck Transport
Landfill
100 Miles
Groundwater Leachate (Negligible)
Leakage (~ 0.02%)
Groundwater Leachate (~ 100%)

Source: Reference 1.

Figure B-3 - Potential Sources of Environmental Release from Disposal of Carbon Tetrachloride Production Wastes in Off-Site Landfill still identify clearly where additional key data should be obtained for a subsequent detailed assessment, or may identify key or additional decision factors that the decision maker may wish to consider in reaching a conclusion. Economies of scale should be reasonably expected as additional scenarios are developed for assessments of a given waste or for many typical wastes, because of the increasing data base and experience gained.

APPENDIX C

ECOLOGICAL AND SOCIOECONOMIC IMPACT ASSESSMENT

Alternative hazardous waste management approaches can have numerous and differing ecological, economic, and social consequences that should be evaluated in a comprehensive risk assessment. The human health risks were the primary concern of the present study, and only brief attention could be given to a review and incorporation of these other impacts. Only a short survey of the literature on such assessment was possible on our study and was not updated during later revisions of this report. Many references are noted, however, which the reader may find useful.

The term "impact assessment" covers several kinds of analyses with different focal interests. These analyses generally involve attempts to make formal and defensible appraisals of the potential consequences of a proposed project, program, action, or decision, particularly the adverse impacts. Familiar examples include environmental, social, economic, energy, regulatory and political impact assessments. At a minimum, potential environmental and socioeconomic consequences can be identified qualitatively; ranking or estimation of the potential magnitudes of adverse impacts can be useful for some decisions. More detailed, quantified and carefully documented analyses could be required for other decisions.

Comprehensive assessments of ecological or socioeconomic impacts can require resources and efforts of similar or greater magnitude than needed for health risk estimation. For example, a procedure developed by the U.S. Geological Survey for evaluating environmental impacts of proposed construction or development projects provided a matrix containing 8,800 elements that could be considered (USGS, 1971). A substantial review and evaluation of the methodologies used for such assessments would require chapters comparable in length to that on health risk assessments, and is beyond the scope of this study.

1. Ecological Impact Assessment

The 1969 U.S. National Environmental Policy Act requires the preparation of environmental impact statements (EISs) on proposed government-related projects. EISs initially tended to be rather site-specific and emphasized the physical and ecological environmental parameters, but later included or gave increased attention to socioeconomic impacts. Environmental impacts assessments now often include for decision options or alternatives the social, economic and aesthetic impacts of technologies or pollutants on communities, structures, artworks, and vistas. Socioeconomic impacts are discussed in the next section.

A wide range of techniques are used in the determination or estimation of the risks of environmental damage by existing or proposed technologies. These methods draw on a substantial body of information in the physical, biological, toxicological, chemical, earth, water resources, and meteorological sciences. Specific approaches can range from counting or estimating populations of various species on various ranges under changing conditions to monitoring and modeling the fate and effect of pollutants and contaminants entering the environment in various quantities and at given points. They can require estimating the bioaccumulation of persistent chemicals in terrestrial or aquatic organisms at the bottom of the food chain, and estimating the accumulation of long-lived gases in the upper atmosphere that may affect the earth's influx of ultraviolet radiation or its thermal balance.

Assessments of the ecological effects of pollutants differ in an important way from assessments of their human health effects: in the latter the analyst attempts to interpret data for several species in terms of the one (i.e., man) while in the former the analyst must extrapolate data for a few species to many (perhaps hundreds of) species. One must also attempt to evaluate the potential synergistic effects of a wide assortment of multiple insults to the environment. Delayed, prolonged, and irreversible effects pose especially difficult challenges. Hence environmental assessments may, at times, require much more data than a health effects assessment, yet provide an answer that is more tenuous or at least less quantitative.

Many types of impacts on nonhuman species are important. These include disturbances of local ecosystems, disruptions on a regional, national, or international scale, impacts on recreational, sport, or commercial fishing, and damages to agricultural and forest crops. One particularly difficult risk assessment problem is that of trying to place values on little-known endangered species (e.g., the small snail darter fish in Tennessee). An even more difficult societal problem has been trying to determine the degree of technological control that should be sought when the intensity of the effect on the nonhuman population is quite uncertain (but possibly large), while the costs of implementing the controls are certainly quite large.

Methods used in specific environmental impact assessments will depend on the technologies considered and the environmental values that may be threatened. Canter (1977, 1982), Kates (1978), and Whyte and Burton (1980) discussed environmental risk assessment in general. Porter et al. (1980) discussed methodologies for impact analysis in general including environmental impact statements. Porter and Rossini (1980) reviewed the methodology for EIA in the context of integrated impact assessment. Barnthouse et al. (1982) and Barnthouse and Suter (1984) examined several methodologies for environmental risk analysis. Conway (1980) presented many papers focusing on analysis of environmental risks of chemicals. Cairns et al. (1978) focused on the effects of chemicals on aquatic life, while Ward (1978) described theory and methods for biological environmental impact assessments. Ott (1978) described the theory and use of environmental indices, while Canter and Hill (1979) and Rau and Wooten (1980) published handbooks helpful in performing environmental impact analyses. Starr et al. (1977), House (1977), and many others examined the environmental impact of energy sources. EPA has recently published water quality criteria for aquatic life (EPA, 1985). A user's manual for ecological risk assessment of synfuels technologies was recently published (Barnthouse and Suter, 1986). EPA's recent guide to the risk literature (EPA, 1987) contains a section on ecological risk assessment that includes references to reports on methodologies).

For assessments of hazardous waste management, a useful approach will likely have steps in common with those used in assessing risks to human health: (1) develop data on release, transport, and fate of chemicals involved; (2) identify species and populations or other values likely to be at risk; and (3) assess impacts on exposed populations or other values. Thus information on the chemicals present and released from the waste and their general physical, chemical, and biological properties usually provides the starting point in both environmental and health effects assessments. In some cases, however, certain routes of release and transport may be less important sources of harmful exposures for natural populations than for humans, e.g., release to deep groundwaters. On the other hand, certain activities may have substantial impact on environmental values that pose little, if any, risk to human health, e.g., disruption of breeding areas for a species ecologically essential in the food chain of the area or of an an endangered species. Hence information about the terrestrial and aquatic ecology of a particular TSDF site is as essential as information on release and transport routes in a comprehensive environmental impact assessment.

Input and output data from the release and transport modeling runs of the health risk assessment will be similarly useful in the environmental assessment. Site characteristics such as topography, depth to groundwater, soil type, vegetative cover, and distance to the nearest body of water are examples of input information that will have been compiled. The transport modeling data are then combined with information on the natural populations present and biological effects data (e.g., fish toxicity and mammalian, bioconcentration, biodegradation, and effects on microflora and microfauna) to develop a qualitative or quantitative estimate of projected impacts.

Computerized models have been developed that contain modules to help assess the environmental risks associated with various waste management practices. One example is the RCRA Risk Cost Analysis Model, also known as the waste-environment-technology or WET model. This model separately estimates the risks posed by the release of waste stream constituents to aquatic and to terrestrial ecological systems (ICF, 1984). It systematically incorporates ecotoxicity data, mostly obtained from single species tests, into a scheme that provides a measure of adverse ecological effects, or "ecorisk." The effects of the hazardous pollutants are scored and stated separately for aquatic and terrestrial ecosystems.

2. Socioeconomic Impact Assessments

Potential socioeconomic impacts are important considerations in regulatory decisions of hazardous waste management alternatives. The EPA has long recognized the need to analyze such impacts (Taylor, 1981). Socioeconomic aspects can include: costs to the regulated industry; economic and social impacts of the hazardous waste management practices on the affected community or region; comparative risk-cost-benefit balance of the options; long-range technological outlook; public perception of the risks and regulatory options; and comparative difficulty in implementing different regulatory options. The socioeconomic impacts can be as influential in decision making, at times, as health impacts, particularly when health risks are uncertain or strongly questioned.

An extensive literature exists on approaches and methods for assessing socioeconomic impacts. These approaches often have features in common, while having different focal points and terminology, and many elements of the methods developed can be useful specifically in hazardous waste decisions (Taylor, 1981). A detailed review and evaluation of this literature is beyond the scope of this report, but a brief overview with references may be useful for many readers. Capsule summaries are given below for three of the better-known approaches: economic, social, and technology assessments. Note that technology assessment, as frequently defined, includes both economic and social effects among others. Also, social effects are often a second order effect of economic impacts. These interrelationships should be noted.

a. Economic impacts: Two major types of economic analyses are used: those which focus on costs to the regulated industry, and those looking broadly at economy related impacts on society, including transnational impacts where appropriate.

Costs to the regulated industry - This type of analysis usually produces quantitative estimates of the costs of a given technological alternative so that comparisons can be made either with present practices or with one or more other technological alternatives. Typically engineering costs are estimated for facilities and equipment, and for annual operating and maintenance needs. Other costs often will be included, such as expenses in developing and submitting data for necessary permits or for meeting monitoring requirements of a regulation.

The costs of alternative technologies can be compared in several ways. A simple approach is to compare total capital and annual operating costs over a given period of use. Another approach compares unit costs, i.e., the total annual operating cost per annual unit output. Since the costs are incurred over time, the present values of the total costs (which takes into account the time value of money) can be a better basis of comparison. Uncertainties may be reduced if the periods of use are identical. The comparison of the present values of the total costs can still be misleading, since technologies have different life cycles. For example, two technologies with identical capital and annual operating costs will have different present values for their costs if they have different time patterns. The annual revenue requirement also can be computed, i.e., funds required to offset the total annual costs of the technology (including interest and tax effects). The costs of the alternative technologies are then compared on the basis of their annual revenue requirements using the same annual rate of return and capital recovery factor for both estimates.

Societal economic impacts - Economic costs to society of a proposed action are more difficult to quantify than are costs to the regulated industry. Economic benefits are at least as difficult to estimate, but often have been of less concern than potential economic costs in most environmental decision making. Particularly difficult to estimate agreeably are the important secondary and tertiary economic benefits to society.

Two subsets of societal economic analyses are Regulatory Impact Analysis (RIA) and Energy Impact Analysis. Interest in RIAs stems from the

1981 Presidential Executive Order 12291, which directs government regulatory agencies to prepare an RIA for every major regulatory rule. Briefly, the order requires that an agency calculate the costs and benefits of the proposed regulation and compare them with the costs and benefits of other approaches to ensure that the proposed approach maximizes net social benefits. Although E.O. 12291 provides some guidance, considerable discussion has ensued over how to identify and compute these costs and benefits, and particularly over how to take risks to human health into account. Interest in energy impacts developed because of the dramatic price rises in oil during the 1970s which affected budgets in the government and private sector and the U.S. balance of trade. Energy impacts are not currently a significant factor in choosing between hazardous waste management alternatives, but could be again in the future.

The methods used in economic impact have been primarily those of cost-benefit analysis, while those used for economic risk analysis have ranged from those developed for personal financial planning to corporate venture decisions, investment portfolio management and international loans, to name but a few. Most of these methods rely on a body of historical statistical data, but often use societal and technoeconomic forecasts of trends and discontinuities, and numerous specialized techniques. The risk analysis methods used in the field of insurance are of special interest, since these must consider life, medical costs, and environmental risks. An extensive literature exists on cost-benefit and cost-effectiveness analyses in a risk assessment perspective (Page and Ricci, 1985).

a. Social impact assessment: Social impact assessment (SIA) developed by analogy with environmental impact assessment and because of the view that many government programs and corporate activities were having adverse effects on society and the quality of life. Social risk assessment has a less developed body of quantitative methodology, at this point, than economic, environmental, or health assessments. The subject area of social impacts tends to be very broad: it ranges from local demographics to the technosocial infrastructure and to our traditions. It touches the fields of sociology, economics, psychology, public health, education, political science, religion, and philosophy. It involves basic cultural and individual questions of ethics and values; a given social consequence may be considered quite adverse by some, but strongly desirable by others. The determination of direction and rate of change of the social "quality of life" is at times much more difficult than in economic or health (and perhaps in environmental) areas. Hence one tends to be much less concerned with small risks in the social impact areas* than in economics or health. Considerable interest has grown in recent years, however, to improve our methods for social accounting and to identify and use a set of "social indicators" for predictive and assessment purposes (Johnston, 1978). One of the simplest and most useful means of visualizing a wide range of potential or hypothetical social problems is through the development of so-called "likelihood-desirability" plots which array estimates for the likelihood of the problem occurring against the desirability or undesirability of possible consequences, assuming that the problem did, in fact, occur.

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* However, note that what might appear to be "small" to society-at-large may appear to be important to individuals or special interest groups. Determination of de minimis risk can be quite controversial in such cases.

A substantial literature is developing on the preparation, content, and uses of SIAs. See: Finsterbush and Wolf (1977), Tester and Mykes (1981), Soderstrom (1981), Wolf (1981), and Leistritz et al. (1982). Risk assessment aspects of the technology-society interface have been discussed by several authors in Conrad (1980), by Wynne (1983), and by many others. A Harris (1980) opinion poll of societal perception of technologically related risk is of considerable interest, as are the studies by Slovic and co-workers (see Fischhoff and references therein (1981), Green (1980), and Vlek and Stallen (1980, 1981). Lawless (1977) described 100 cases of social shocks from diverse technologies, including several that involved hazardous chemicals or wastes. EPA's recent guide to the risk literature does not include a section on socioeconomic risk assessment, but does contain sections on corporate risk assessment and legal aspects of risk assessment, management, and communication (EPA, 1987).

c. Technology assessment: Technology assessment is a systematic and iterative anticipatory study of the broad range of consequences for society of technological change and of alternative technology policies. It emphasizes identification and analysis of those policies for technological development that are consistent with national goals* and gives particular attention to those consequences that may be unintended, indirect, or delayed. The thrust of technology assessment is, therefore, not exclusively on technological competitiveness, but rather on the management of technology in the public interest by government and private sector parties. Technology assessment draws on techniques and methods from several research areas such as technological and social forecasting, modeling, systems analysis and policy analysis, but it is not a standardized step-by-step methodology. Practitioners tend to structure a methodology appropriate for the particular technology and data base. The product of a technology assessment is a systematic organization of what is known (and what needs to be known) about a new or growing technology, its potential consequences for the environment, human health and social institutions, and the probable effects of alternative policy decisions pertaining to its development or control. In short a "TA" is a technosocial impact statement that should serve as a platform for discussion and decision making concerning allocation of research resources, developing regulatory strategies or legislative policies, and setting priorities. See also: Hetman (1973), Armstrong and Harman (1977), Martino et al. (1978). and Porter et al. (1980).

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* A reviewer has noted that while national goals are of concern to TA, distributive justice concepts are also important at international, regional, and local interest group levels. Indeed, national goals are often ill-defined and complex in their interrelationships because of numerous relevant trade-off concepts.

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